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PRINCIPAL INVESTIGATOR: Ralph Gill

CONTRACTING ORGANIZATION: Ardiem Medical, Inc.
Indiana, PA 15701

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13. ABSTRACT (Maximum 200 Words)

Recent work in the field of emergency and therapeutic hypothermia shows excellent results through the induction of mild-to-moderate profound hypothermia (SA) in laboratory animals using devices developed and fabricated by Ardiem Medical, Inc.

An engineering prototype of a device used for the induction of mild- (34°C) to-moderate (30°C) hypothermia was delivered to Safar Center for Rescuscitation Research (SCRR) in the last reporting period (01 Sept. 2002 – 31 Aug. 2003). This prototype induces *mild-to-moderate hypothermia* via a venous or arterial shunt for use in cases where the patient exhibits spontaneous circulation. An engineering prototype device used for the induction of ***profound hypothermia*** (10°C - 20°C) was delivered to SCRR in December 2003. Profound hypothermia, induced by a flush of a large volume of chilled fluid via the thoracic aorta toward the heart and brain with drainage from the right atrium, is for use in cases of cardiac arrest resulting from trauma-related exsanguinations.

Ardiem Medical, Inc. used results obtained in SCRR's animal testing program and in engineering-protoype bench testing at Ardiem to reiterate the design and update both device prototypes. This information was also used to revise the design requirements documents, an updated engineering prototypes of both devices were delivered to SCRR in September 2004.

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Table of Contents

FINAL REPORT

AWARD NO: DAMD17-01-2-0051

PRINCIPAL INVESTIGATOR: Ralph Gill, BSME

INSTITUTION: Ardiem Medical, Inc.

TITLE: Devices for Emergency Hypothermia and Military Applications

Introduction

Recent work in the field of emergency and therapeutic hypothermia[1,2,3,4,5] conducted by the Safar Center for Resuscitation Research (SCRR) shows excellent results. Part of the SCRR work is based on induction of mild-moderate or profound hypothermia (SA) in laboratory animals using devices developed and fabricated by Ardiem Medical, Inc.

An engineering prototype of a device used for the induction of mild (34°C) to moderate (30°C) hypothermia was delivered to SCRR in August 2003. Mild to moderate hypothermia is induced via a venous or arterial shunt for use in cases where the patient exhibits spontaneous circulation. An engineering prototype device used for the induction of profound hypothermia (10°C - 20°C) was delivered to SCRR in December 2003. Profound hypothermia is induced by a flush of a large volume of chilled fluid, via the thoracic aorta, toward the heart and brain, with drainage from the right atrium. Profound hypothermia induction is for use in cases of cardiac arrest resulting from trauma-related exsanguinations. The purpose of these original engineering device prototypes was to aid the SCRR staff in their research and to provide Ardiem Medical, Inc. with feedback for refining these devices.

Ardiem Medical, Inc. used results obtained by bench testing of the engineering prototypes, plus results on animal testing at the SCRR, and recommendations by the SCRR staff to reiterate the design and update these device prototypes. This information was also used to revise the design requirements documents. Updated engineering prototypes of both devices were delivered to SCRR in September 2004.

The next generation of these devices will be clinical prototypes for hospital use (ER) and will be designed and built to meet the updated design requirements. The clinical prototypes will be used for human testing, and clinical trials, and are due for delivery in the first half of 2005.

In addition Ardiem Medical, Inc. conducted an investigation regarding the feasibility of designing portable devices for field use: a) for profound hypothermia induction in the battlefield, b) for profound hypothermia induction in emergency vehicles, c) for mild-moderate hypothermia induction in emergency vehicles, and d) combination profound/mild-moderate hypothermia induction device in emergency vehicles. An engineering prototype of a combat profound hypothermia induction device is available but not fully tested. The prototype was delivered to SCRR also in September 2004. An engineering prototype of a profound hypothermia induction device for emergency vehicle (EV) use is scheduled for delivery in the second half of 2005. An engineering prototype of a mild-moderate induction device for emergency vehicle use is scheduled for delivery in 2006, with a possible combination device, also for emergency vehicle use, to follow.

Body

Mild to Moderate Hypothermia Induction Devices

The goal of mild (34°C) or moderate (30°C) hypothermia induction is to lower the core body temperature under spontaneous circulation via shunt blood flow after cardiac arrest, traumatic brain injury, acute stroke, spinal cord injury, etc. and during surgical procedures. The induction of mild or moderate hypothermia has been shown to decrease the damage to organs, specifically the brain, during low blood flow. Several access techniques for inducing mild hypothermia are available depending upon the specific situation and are discussed by SCRR. The variations do not materially affect the device design or configuration.

The basic requirements of the device as underlined in the original design requirements document are:

1. To chill deviated blood in shunt to a minimum of 6°C (lower causes damage) for the purpose of gradually reducing body core temperature to a selectable 34°C or 30°C.
2. To maintain core body temperature at 34°C or 30°C.
3. To circulate deviated blood in shunt at a flow rate of up to 500 mL/min.
4. To be used in a hospital trauma emergency room setting with electrical power requirements that are consistent with that available in the hospital. That is 120 VAC at up to 20 A.

Two engineering prototypes of this device (see Figure 1) were designed and built. The first prototype was delivered to SCRR for animal testing and evaluation in August 2003 and the second was kept for testing and refinements.

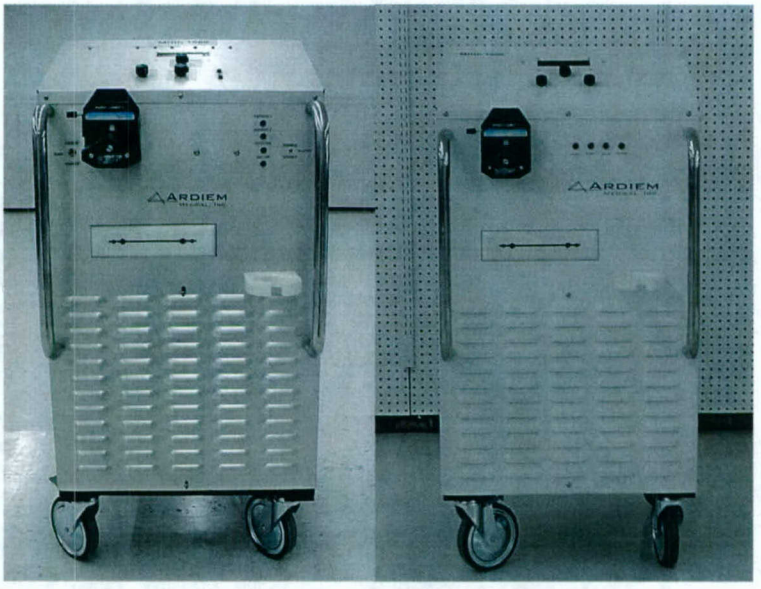

Figure 1. Photograph of the first (left) and second mild-moderate engineering prototypes.

To meet the cooling requirements of 1 and 2 above, it was determined (see previous report) that the system must pump 1300 W of heat, plus heat gained from ambient, for a total of 1600 W and maintain a constant temperature. Controlling of the evaporator temperature, blood temperature, and the body temperature, by cycling the compressor on/off was dismissed because it would result in large swings in temperature and cause

inrush currents. Instead, a method of controlling the evaporator temperature through control of the system cooling capacity was chosen.

Among the relevant control methods, the indirect hot-gas bypass method was chosen. The concept is depicted in Figure 2. This method uses a controllable bypass from the high-pressure side with the injection occurring between the expansion valve (TEV) and the evaporator. In the high demand mode, the bypass remains closed and the system supplies its full output. If the demand falls, the controller continuously opens the hot-gas bypass valve. Hot-gas now flows through the bypass to the evaporator inlet where it mixes with the liquid refrigerant and is cooled. As the liquid evaporates the vaporization temperature rises, thus lowering the system output. The indirect bypass control is the best choice because it is simple and reliable. To be effective, the expansion valve must be capable of controlling the refrigerant supply (R134a) from 100% to the minimum load requirement

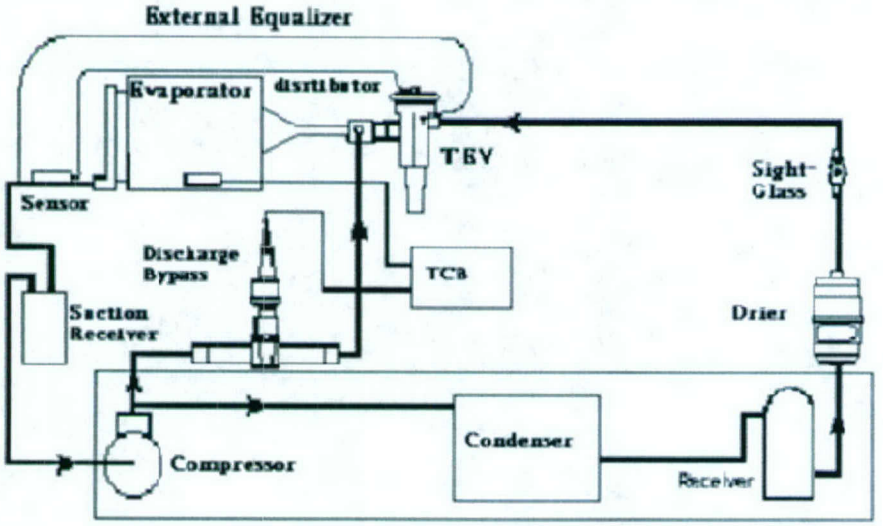

Figure 2. Block diagram of indirect hot-gas bypass control concept.

The chosen compressor/condenser was capable of pumping 2010 W at 7.2 evaporator and 32.2°C ambient temperatures while operating at 120 VAC with maximum current draw of 18 A.

Blood must be chilled through the evaporator from 37°C to approximately 6°C, at a flow rate of 500 mL/min. The evaporator (see Figure 3) consists of a primary heat exchanger and a secondary heat exchanger. The secondary, which is part of a disposable tubing set, must be sterlilzable and heparin bondable. Existing heat exchangers intended for the cooling of blood are not capable of cooling to the extent required for the induction of mild hypothermia within the time frame desired. Therefore custom primary and secondary heat exchangers were designed and constructed. The required size of the bag was calculated to be100 mm x 265 mm (3.94 in x 10.43 in).

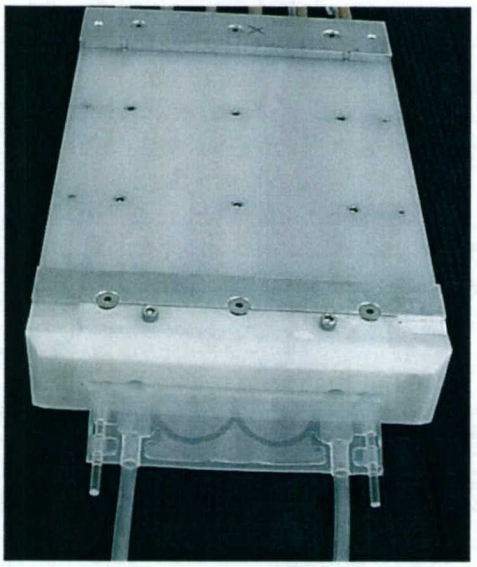

Figure 3. Photograph of the evaporator consisting of a primary heat and a secondary heat (fluid bag partially inserted) exchanger.

System bench testing at Ardiem Medical, Inc. and testing on animals at SCRR showed a body cooling rate that exceeded expectations but also revealed some problems. The most critical problem was not being able to stabilize the patient temperature at mild (34°C) or moderate hypothermia (30°C) to within +/-0.5°C. Also returning to normothermia[1] (37°C) could not be accomplished. To resolve these problems a pair of Kapton foil heaters was added to the evaporator. In addition a reduced amperage (15.5 A) and cooling power (1680 W at 7.2°C evaporator and 32.2°C ambient temperatures) condensing unit was chosen to allow both compressor and heaters to be powered on all the time. The evaporator plates were reduced in thickness and polypropylene was used for the outer top and bottom plates instead of aluminum in order to reduce the mass and speed the response. Also, fluid bags, which were increased in length by two inches, were designed and custom fabricated.

The original heating requirements were calculated as follows:

Heat exchanger mass: 9.5 x 14 x 2.125 = 332 cu in or 33lbs.

Thermal capacity of aluminum: 0.214 BTU/lb -°F (9/5) = 0.38 BTU/lb-°C.

Thermal capacity of exchanger: C = 0.38 (33lb) = 12.5 BTU/°C.

Raising the temperature of the evaporator from 0°C to 50°C (ΔT = 40°C), requires

12.5 x 50 = 625 BTU or 183 W-hr.

Two 4 in X 12 in heaters of 4 W / sq in power density, will provide

2 x 4 x 12 x 4 W = 384 W

and will raise the temperature in

---

[1] Return to normothermia requires heating of blood and was not included in the original design requirements.

183 W-hr / 384 W = 0.476 hr or 28.6 min.

Total current drawn by the heaters at full power is equal to

384 W / 120V = 3.2 A.

The heater design and placement, plus the control algorithm for heating and cooling (see Appendix A for details) took a few iterations to yield optimum results. We decided, in order to avoid damage to blood, to control the blood inflow temperature (infused to the body) to 10°C for hypothermia or 42°C for normothermia until the body temperature reaches the set point +/-0.5°C then switching to controlling the body temperature to the set point (see Appendix B for details). The new design was tested and was found to be capable of stabilizing the body temperature to within +/-0.5 of the set point albeit at a slower cooling rate. That is 0.226 °C /min versus 0.326 °C /min for a flow rate of 500 mL/min and for a body mass of about 25 kg observed in the first engineering prototype. In addition, it was requested by the SCRR to increase the selectable flow rate from 500 mL/min maximum to 1000 mL/min maximum, and to determine the effects of expanding /contracting the tubing ID and the effects of the increased flow rate at high/low fluid temperatures, and accurately calibrate the flow rates. Initially the flow rates were off because the NIST traceable calibration instrument we used to obtain reference readings was malfunctioning (see Appendix C). Testing was carried out (see Appendix D) and found that the pump could accommodate faster flow rates up to 900 mL/min and the compressor was of sufficient cooling power to accommodate the faster flow rates. Eventually all SCRR requests were granted. As a result, the second engineering prototype was updated with these changes and with the new temperature control approach.

SCRR also requested the inclusion of a bubble detector and provisions for fluid pressure measurement and display. These requests were addressed (see Appendix E and Appendix F), but the changes were not incorporated in the second engineering prototype because of the extensive additions to the electronics it would have required. However they will be incorporated in the clinical prototypes that will be designed and built to meet the specifications underlined in the design requirements document (see Appendix G), which was revised as a result of the testing and recommendations by SCRR.

Because of the reduced current draw, the clinical prototypes for hospital use will utilize an attractive graphical user interface. However operation at 120 VAC and just under 20 A, plus the large size and weight of the components makes direct transition to a portable device practical only for large emergency vehicles (see Appendix H for details). Therefore, the vapor compression refrigeration method does not lend itself to miniaturization. For this reason the CO_2 refrigeration method was revisited and tests were carried out to determine applicability (see Appendix I). Initial testing shows promising results as enough energy exists in a 20-lbs compressed CO2 cylinder to induce mild hypothermia to a 75 kg person at a rate comparable to that of mechanical refrigeration. Therefore a device that utilizes CO_2 cooling and operating on a 12 V battery (good for $1^1/_2$ hours of procedure), weighing about 70 lbs, and measuring 2.5ft x 3ft x 1ft (see Appendix J), not including the compressed CO_2 cylinder, is feasible. A 20-lb compressed CO_2 cylinder weighs about 45 lbs when fully charged and measures 9" diameter X 28" height.

Profound Hypothermia Induction Devices

Profound hypothermia is intended for use primarily in cases of trauma-induced exsanguination cardiac arrest. In these cases, which are considered unresuscitable by standard methods, the profound hypothermia (suspended animation), with or without drugs, is intended to preserve the organs for delayed resuscitation, organ repair, or organ harvesting.

The induction of profound hypothermia is accomplished by a rapid one way flush with a large volume of cold fluid via the thoracic aorta toward the heart and brain, with drainage from the right atrium.

The basic requirements of the device as underlined in the original design requirements document are:

2. To maintain 20 L of fluid to –5 to + 5°C (isotonic saline solution is presently used while other fluids are to be researched and or developed by SCCR and others)
3. To deliver the fluid by means of a pump at up to 2 L/min via a disposable and sterile tubing set and a catheter.
4. To be used in a hospital trauma emergency room setting and the power requirements are to be consistent with that available in the hospital.

Two engineering prototypes of this device (see Figure 4) were designed and constructed. The first prototype was delivered to SCRR for animal testing and evaluation while the second was kept at Ardiem Medical, Inc. for testing and refinements.

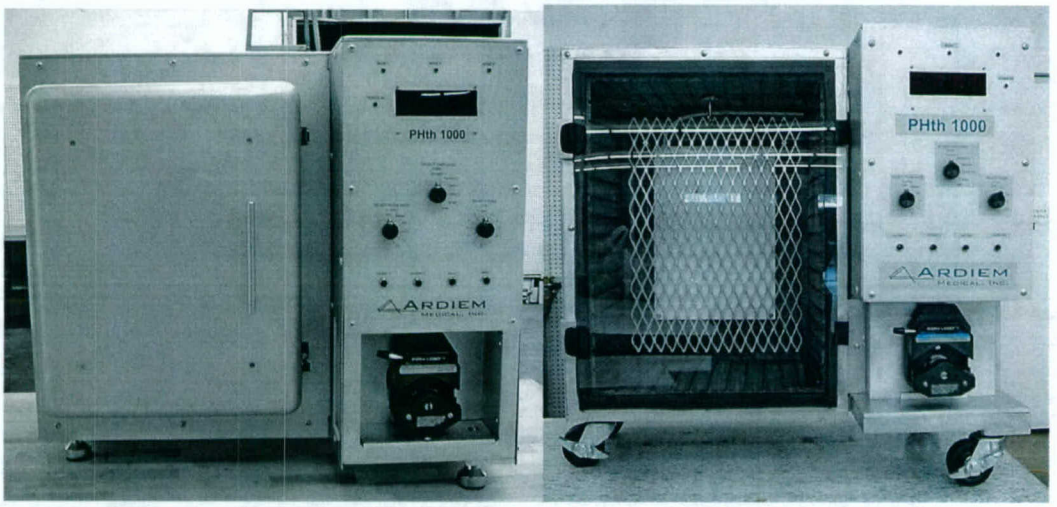

Figure 4. Photograph of the first (left) and second profound (updated) engineering prototypes.

To meet cooling requirement 1, an insulated cold box was needed with an evaporator and a small 20 W, 12V DC condensing unit (a 50 W was chosen, see previous report) for maintaining the fluid inside the diffusion cold bag. Controlling the fluid temperature to the set point requires accurate fluid temperature measurement. A suitable medical grade skin temperature probe was chosen and tested for this application (see Appendix K).

System bench testing at Ardiem Medical, Inc. and testing on animals at SCRR (see Appendix L and Appendix M) showed results to be within expectations and the device to be operating within specifications. However the SCRR requested some testing and enhancements to the device such as: a) determination of the effect of fluid temperature on flow rate, b) accurate calibration of the flow rates, c) transparent cold box door to allow viewing of the fluid level in the diffusion bag, d) inclusion of a bubble trap/filter e) inclusion of a bubble detector, and f) fluid pressure measurement and display. Subsequent testing was carried out (see Appendix D, Appendix E, and Appendix F) and all these requests were granted. As a result, the second engineering prototype was updated with changes a) – d) and tested successfully (see Appendix N) but not with changes e) and f) because of the required extensive additions to the electronics. However these changes will be incorporated in the clinical prototypes that will be designed and built to meet the

specifications underlined in the design requirements document (see Appendix O), which was revised as a result of the testing and recommendations by SCRR.

Because all components of this device operate at 12 VDC and draw a small amount of current, a) it is a simple task to transition this device to a portable version and b) it allows for the clinical prototypes for hospital use to utilize an attractive graphical user interface (see Appendix H for details). The concept and feasibility of a portable profound hypothermia induction device based on vapor compression refrigeration for emergency vehicle use is presented in Appendix P while preliminary design requirements are listed in Appendix Q.

It is uncertain whether the above unit will be applicable for battlefield use. For a unit in the form of a backpack for battlefield use, the weight of the cold box and refrigeration system are excessive, as maximum load was determined to be 70 lbs. The weight of a filled 20-liter fluid bag alone is about 45 lbs. Therefore if pre-chilled fluid is available for use and the fluid bag is placed in a chamber with good insulation, refrigeration is not needed. After assessing insulation materials and successful testing (see Appendix R for details), Ardiem developed a concept and determined the feasibility of a combat profound hypothermia induction device (see Appendix S). Ardiem also developed preliminary design requirements for such a device listed in Appendix T. An engineering prototype (see Figure 5) of such a device was designed and fabricated. The unit is packaged in a backpack and weighs 22 lbs excluding the fluid. Preliminary testing shows that the unit holds 20 liters of fluid to within 5°C for 6 hours with battery power enough for six procedures before recharging.

We also looked at the possibility of utilizing CO_2 as refrigerant in cooling the fluid on the fly while being infused using the same evaporator plates of the mild-moderate unit. Therefore using CO_2-liquid phase instead of recycled Freon. A device built on this premise does not require a condensing unit and may be designed with 12 VDC components with low electrical power requirements. Therefore it can be of much reduced weight and size and capable of operating on battery power. However we encountered problems with CO_2 freezing when released at the fast rates needed to cool the fluid sufficiently (below 5°C) at 2 L/min. When liquid CO2 is passed through a pressure-dropping orifice to atmosphere or near-atmosphere conditions, the flow becomes a combination of gas and entrained solid dry ice particles, that under high-flow conditions, can clog the low pressure piping if no heat is allowed to warm the pipe via natural or forced convection from the environment (see Appendix I for details). Therefore more work is needed for a modified evaporator. Also, because a large volume of CO_2 is needed, which is an oxygen displacer, a device based on this method of cooling can only be used outdoors.

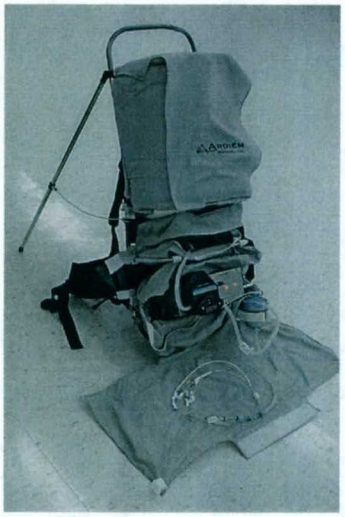

Figure 5. Photograph of the combat profound hypothermia induction device engineering prototype.

Hybrid Device

The idea of combining the two units into a single portable unit that could be used to induce either mild/moderate or profound hypothermia was included in the original proposal. One approach is to merely combine the two existing units into one. However the resultant unit would be too heavy and bulky and require 120 VAC for operation. To miniaturize such a unit for portability, the best approach is to rid the cold box and refrigeration system of the profound unit and rely on cooling the blood or the fluid with a heat exchanger similar to the mild-mod unit. We tested, as a first step, the second mild-moderate engineering prototype to determine whether it would chill the fluid sufficiently on the fly (see Appendix U). To be effective in inducing profound hypothermia, the fluid temperature must be reduced to below 5°C. The cooling power of this device was not sufficient to chill the fluid to this level at the fast flow rate of 2 L/min required for profound hypothermia induction (note that it is estimated that 3000 W of cooling power is required). The cooling power was not sufficient even at 1 L/min. As a second step we tested using CO_2 as the refrigerant (see Appendix I). Subsequently a concept was formulated for the possible configuration of a hybrid portable device. Such a device will utilize CO_2, operate on a 12 V battery, weigh about 100 lbs including the weight of the 20 liters of fluid, and measure 2.5 ft x 3 ft x 1ft. The compressed CO2 cylinder is not included. We established that such a device can be used to induce mild-moderate hypothermia (Mild-Moderate Hypothermia Induction Devices section) however, the feasibility of such a device hinges on more testing as described in the Profound Hypothermia Induction Device's section.

Test Fixtures

In the course of bench testing at Ardiem Medical, Inc., the need of a test subject for testing cooling or heating device capabilities became obvious. We therefore designed a thermodynamic equivalent of a 25 kg body (see in Appendix V for details).

Also for testing the calibration of the measuring electronics, we designed a temperature calibrator. The calibrator accuracy was found by testing to be comparable to a NIST traceable instrument (see Appendix W for details).

Key Research Accomplishments

- Designed and constructed non-portable mild-to-moderate prototypes (2) that were successfully tested in SCRR laboratory animal studies

- Refined and reiterated the design of, and upgraded the laboratory mild-moderate hypothermia induction device, based on the test data generated by laboratory testing at Ardiem and at SCRR on animals.
- Generated design requirements of the mild-moderate hypothermia induction device for hospital use (ER).
- Researched the CO2 cooling method for application and ways of miniaturizing and simplifying the mild-moderate hypothermia induction device to create a portable device suitable for field use.
- Designed and constructed non-portable profound prototypes (2) that were successfully tested in SCRR laboratory animal studies
- Refined and reiterated the design of, and upgraded the laboratory profound hypothermia induction device, based on test data generated by laboratory testing at Ardiem and at SCRR on animals.
- Generated design requirements of the profound hypothermia induction device for hospital use (ER).
- Researched techniques for miniaturizing and simplifying the profound hypothermia induction device in order to create a portable device suitable for emergency vehicle use.
- Generated preliminary design requirements of the profound hypothermia induction device for emergency vehicle (EV) use.
- Researched techniques for miniaturizing and simplifying the profound hypothermia induction device to create a portable device suitable for combat use.
- Generated preliminary design requirements of the profound hypothermia induction device for battlefield use (combat).
- Designed and fabricated a prototype of the combat profound Hypothermia Induction device.
- Researched the CO2 cooling method for application in a combination (profound/mild-moderate) portable device suitable for field use.

Reportable Outcomes

See the body of this report.

There are no technical publications in connection with this work by Ardiem Medical, Inc. However the device use and performance has been and will be reported in SCRR publications.

Two provisional patent applications for devices that induce mild-moderate and profound hypothermia were submitted to Patent and Trademark Office on May 21, 2004.

Conclusions

The conclusions that result from this work are:

- Fabrication and verification of mild-moderate and profound hypothermia induction devices for hospital use that use existing and proven technology has been established.
- Fabrication of portable profound hypothermia induction devices for emergency vehicle and battlefield use that use existing and proven technology is feasible.
- Fabrication of portable mild-moderate hypothermia induction devices for emergency vehicle and battlefield use that use existing and proven technology is feasible.
- Fabrication of portable combination profound/mild-moderate hypothermia induction device for field use may be feasible.

Personnel

Personnel participating and receiving pay from this research effort:

Cupp, James	Research Engineer
Gill, Ralph	Mgr. Mechanical Engineering
Mack, Lenny	Mfg. Machinist
McMurry, Dave	President
Novak, William	Sr. Mechanical Engineer
Park, Christina	Electronics Engineer
Pitsakis, Mike	Mgr. Electronics Engineering
Schendel, Doug	Sr. Mechanical Engineer
Stiles, Wayne	Mfg. Engineering Technician
Rietscha, Scott	Mfg. Assembler
Zhuze, Vladimir	Sr. Software Engineer

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Appendices

A. Practical PID Feedback Temperature Control

B. Temperature Control of Mild-Moderate Hypothermia Induction Device.

C. Evaluation of the accuracy of the OMEGA FLR-1600/FLV-4600 series water flow meter.

D. Flow Rate Accuracy in Mild-Mod BTP and Profound EP 2.

E. Bubble Detection Definitions and Evaluation.

F. Evaluation of Pressure Measuring Components and Measurement of Pressure Ranges In Hypothermia Devices.

G. DRD Mild-Mod Hypothermia Induction Device for Hospital Use.

H. Current Draw of Hypothermia Induction Devices and Effect on Portability.

I. CO_2 Cooling Capability for Mild-Moderate and Profound Hypothermia Devices.

J. Concept and Feasibility of a Mild-Moderate Induction Device for Emergency Vehicles.

K. Skin Temperature Probe Suitability for use in Profound Hypothermia Induction Device.

L. Temperature Control Testing of The First Profound Hypothermia Induction Device Prototype.

M. Temperature Control Testing of the Second Profound Hypothermia Induction Device Prototype.

N. Temperature Control Testing of the Refined Profound Hypothermia Induction Device Prototype.

O. DRD Profound Hypothermia Induction Device for Hospital Use.

P. Concept and Feasibility of a Profound Induction Device for Emergency Vehicles.

Q. DRD Profound Hypothermia Induction Device for EV.

R. Temperature Loss Comparison with several types of insulators.

S. Combat Profound Induction Device Concept and Feasibility.

T. DRD Profound Hypothermia Induction Device for Combat.

U. The affects of using the Mild-to-Moderate device for both mild-to-moderate and profound hypothermia applications.

V. Thermodynamic Simulator of a Pig.

W. Hypothermia Devices Temperature Calibrator.

ARDIEM

Appendix A
TECHNICAL REPORT

Technical Report x.dot

RECORD NO.

AM-00010

TITLE OF TECHNICAL REPORT		REVISION
Practical PID Feedback Temperature Control		01
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2003-01	11/25/03
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Temperature Control	Mike Pitsakis	
TECHNICAL AREA		
Electronic Control		
SUBJECT AND KEY TECHNICAL WORDS		
Control Systems, Automatic Control, PID Control, Feedback Control		

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☒ Other

ASSOCIATED REPORTS

Abstract

The information I provide in this technical report is a compilation and synopsis of material from several reliable sources. It is meant to provide a practical approach for designing and analyzing analog and digital proportional-integral-derivative (PID) feedback controllers based on theoretical concepts. I assume that the controlled process is temperature but can be adapted to any other process. To facilitate the design/analysis, I also created some spreadsheets and PSpice programs described in the body of the report.

Background

System Theory of Feedback Control

A generalized block diagram of a control system[1,2] is shown in Figure 1. In Laplace domain, $G_p(s) = T_o(s)/C(s)$ describes the process we need to control, $G_c(s) = C(s)/T_e(s)$ describes the controller we use to do the job, and $G_f(s) = T_f(s)/T_o(s)$ describes the scaling done to the output signal in order to produce the feedback temperature $T_f(s)$. Where $T_{sp}(s)$ is the input temperature (set point), $T_o(s)$ is the output temperature that we aim to regulate, $T_e(s) = T_{sp}(s) - T_f(s)$ is the error temperature, and C(s) is the controller output.

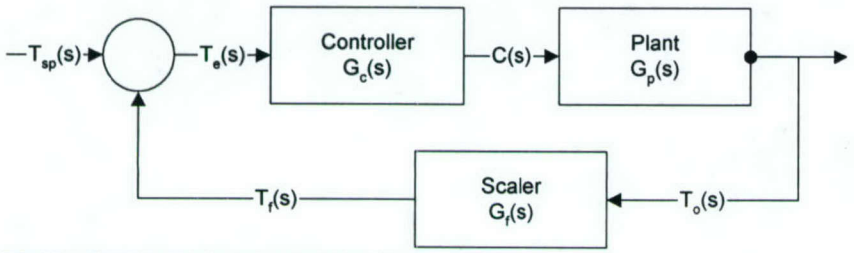

FIGURE 1. GENERALIZED BLOCK DIAGRAM OF CONTROL SYSTEM

The transfer function of the feedback system is given by

$$G_{sys}(s) = T_o(s) / T_{sp}(s) = G_c(s)\, G_p(s) / [1 + G_c(s)\, G_p(s)\, G_f(s)].$$

Often $G_f(s) = 1$ and so $T_f(s) = T_o(s)$. All signals represent temperatures except for C(s) which represents some other quantity such as current in the case of a thermoelectric cooler or a heater or a valve opening percentage in case of a linear valve. Therefore the controller converts temperature to current or valve opening while the plant converts current or valve opening to temperature.

We will restrict the discussion to plants that exhibit a linear first order response with delay and controllers of PID type. So

$$G_p(s) = K_p\, e^{-Td\, s} / (sT_r + 1) \text{ and } G_c(s) = K_c\,(1 + 1/s\tau_i + s\tau_d).$$

Or in time

$$T_o(t) = K_p\,(1\text{-}e^{-(t\text{-}Td)/Tr})\, C(t) \text{ and } C(t) = K_c(T_e(t) + 1/\tau_i \int T_e(t)dt + \tau_d\, dT_e/dt)$$

Where K_p is the plant gain (temperature/current or valve opening) and K_c is the controller gain (current or valve opening/ temperature) and the proportional coefficient $P = K_c$. Where τ_i and τ_d are respectively the integral and derivative time constants of the controller that result to $I = K_c/\tau_I$, the integral coefficient and $D = K_c\tau_d$, the derivative coefficient. T_d represents the delay in plant response and T_r is the time constant of the plant response.

The controller gain may be written as

$$G_c(s) = K_c\,(s\tau_1 + 1)\,(s\tau_1 + 1) / s\tau_I$$

if $\tau_i = \tau_1 + \tau_2$ and $\tau_d = \tau_1\tau_2 / (\tau_1+\tau_2)$. This condition can be satisfied, among others, by $\tau_i = {}^1/_2\,\tau_1 = {}^1/_2\,\tau_2$. Hence $\tau_i = 4\tau_d = T_d$

To get an idea of what the transient response of the system will be, we need to evaluate the transfer function. In order to do that, we use a first order Pade approximant of the delay $e^{-Tds} = (1 - sT_d/2)/(1 + sT_d/2)$ and letting $G_f(s) = 1$, we get

$$G_c(s)\, G_p(s) = G_c(s)\, G_p(s)\, G_f(s) = [K_c\,(s\tau_i/2 + 1)\,(s\tau_i/2 + 1) / s\tau_I]\,[K_p\,(1 - sT_d/2)/(1 + sT_d/2)\,(sT_r + 1)].$$

By setting $\tau_I = T_d$, we cancel one zero-pole pair that simplifies things tremendously and after a lot of math we get,

$$G_{sys}(s) = N(s) / (s^2 + 2\zeta\omega_n s + \omega_n{}^2 s).$$

N(s) is the numerator polynomial. Where ω_n is the natural frequency of the system and ζ is the damping parameter.

$$\omega_n = 2 / \tau_i (4\lambda - 1)^{1/2}$$

$$\zeta = 1 / [(4\lambda - 1)/\lambda)(T_r / T_d)]^{1/2}.$$

Where $\lambda = T_r / (T_d K_c K_p) > ¼$ or $K_c K_p < 4T_r/T_d$.

This system will produce sustained oscillations in response to a unit step input ($T_{sp}(s) = 1 / s$) if $\zeta = 0$ while will be too slow if $\zeta \geq 1$. The response to a unit step input in time for $0 < \zeta < 1$ will be

$$T_o(t) = 1 - [e^{-\zeta\omega nt} /(1-\zeta^2)^{0.5}] \sin\{[\omega_n(1-\zeta^2)^{0.5}] t + \tan^{-1}[(1-\zeta^2)^{0.5}/\zeta)]\}.$$

This is plotted in Figure 2 for $0.4 \leq \zeta \leq 0.9$. Values of ζ below 0.4 and above 0.9 are not used because of the excessive overshoot or the overly sluggish response respectively.

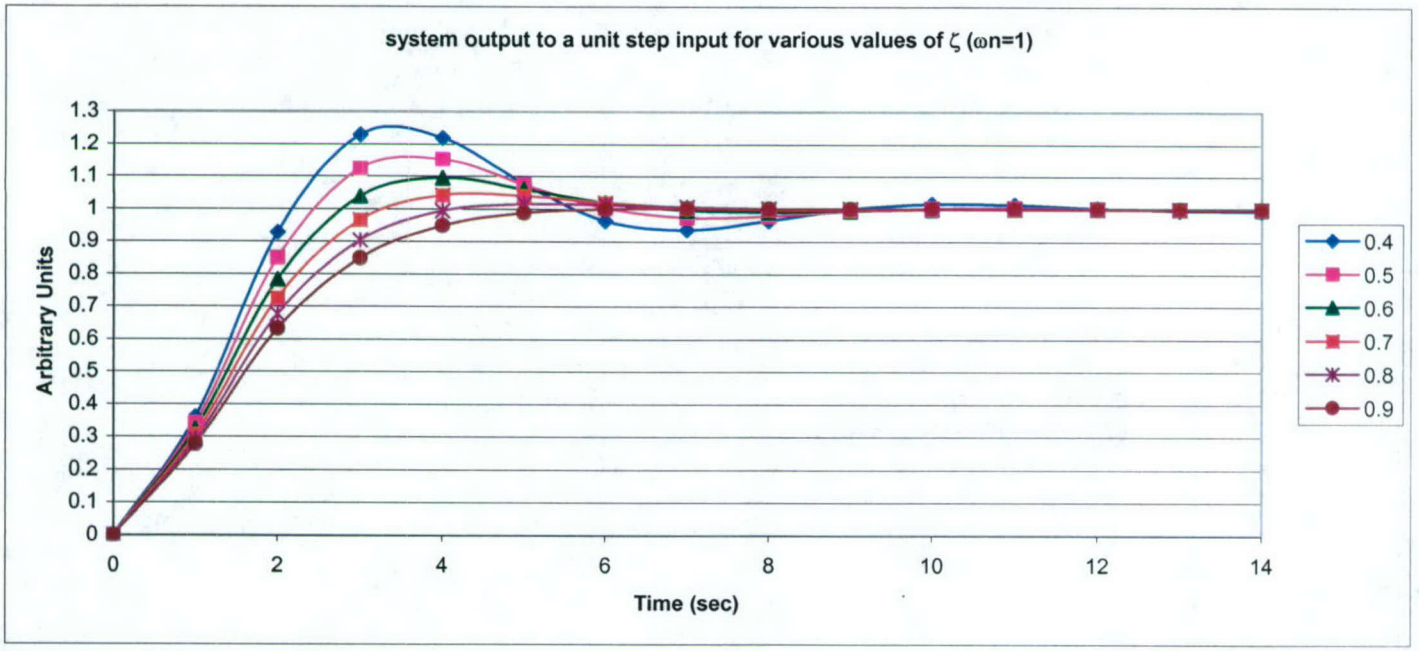

FIGURE 2. SYSTEM RESPONSE TO A UNIT STEP INPUT

The maximum overshoot is given by $M_p = 100\%\ e^{[-\pi (\zeta / (1- \zeta 2)]}$ and occurs at time $t_p = \pi / \omega_n(1-\zeta^2)^{0.5}$. The settling time is given by $t_s = k / \zeta\ \omega_n$, with k equal to 3, 4, and 5 for 5%, 2%, and 1% overshoot respectively. Therefore the response to a step change in set point presents a trade off between amount of overshoot and settling time. However since the overshoot does not depend on ω_n, setting ζ close to 0.9 and ω_n as large as possible will minimize the overshoot and speed up the response.

We now want to know how effective the controller will be to a step change in set point input ($T_{sp}(s) = T_{sp0} / s$) and to a ramp change in set point input ($T_{sp}(s) = T_{sp0} / s^2$) after all transients subside. To this effect we will use the final value theorem:

$$T_{ofv} = \lim_{t->oo} [T_o(t)] = \lim_{s->0} [sG_{sys}(s)T_{sp}(s)].$$

For a step input

$$T_{ofv} = T_{sp0} \text{ for PI or PID control and}$$

$$= T_{sp0} K_c K_p / (1 + K_c K_p) = T_{sp0} / (1 + \lambda T_d/T_r) \text{ for P only control.}$$

We see that the output, in response to a step change in set point, will settle to the set point T_{sp0} if we use PI or PID control but if we use P only control, there will be an offset in output (albeit small because usually $T_d << T_r$ or can be made small with a small λ).

For ramp input, the output will follow the input ramp with some delay if we use PI or PID control and therefore there will be an offset. However if we use only P control, the output will increase much faster than the set point.

Notice that if were not to use feedback and use P control only the final value of the output will be

$$T_{ofv} = \lim_{t\to\infty} [T_o(t)] = \lim_{s\to 0} [sG_c(s)G_p(s)T_{sp}(s)]$$
$$= K_c K_p T_{0sp}$$
$$= T_{sp0} \text{ for } K_c = 1/K_p$$

Hence the error will depend on how well the gains match. Also this is a single point solution that will work as long as there are no disturbances involved such as changes in environmental temperature or changes in load that are unavoidable. The integral part of the control is necessary to avoid offsets. The derivative is not necessary. However it speeds up the response at the expense of adding quick transients at the times of step changes of the input and is needed to stabilize plants that tend to oscillate in response to a step (higher order). It is therefore advantageous to use feedback PI or PID control because it enables as to manipulate system parameters and tailor the response to some extend.

Analog Control Implementation

Analog control refers to control implementations that utilize analog hardware. A block diagram of an analog controller is shown in Figure 3. Here all signal are voltages with the exception of C(s), which may be voltage current or some other signal.

The set point voltage V_{sp} is compared to the amplified feedback signal, V_{fb} to produce the error signal, V_{error}. The controller G_c processes the error signal and produces the control signal, C. The control signal, after power amplification by the driver block, drives the plant designated by block, G_p. Assuming temperature being the process to be controlled, the output temperature reading is expressed as voltage V_{therm}, that is amplified by G_f to produce V_{fb}. G_p will be the heat path between the heater/cooler and the thermistor. Exact knowledge of G_p is not necessary as long as it is a linear first order system.

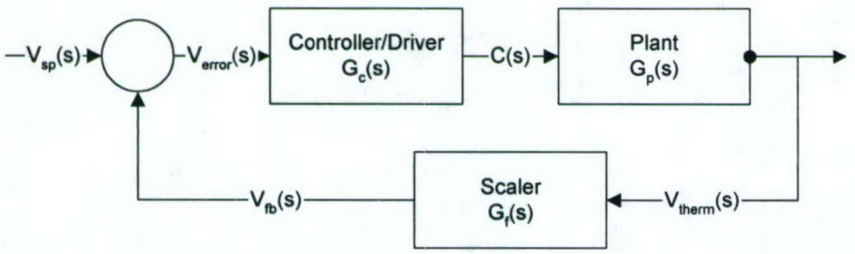

FIGURE 3. ANALOG CONTROL SYSTEM

The following relationships describe such a control system:

$$G_{sys}(s) = V_{therm}(s) / V_{sp}(s) = G_c(s)\, G_p(s) / [1 + G_c(s)\, G_p(s)\, G_f(s)]$$
$$V_{error}(s) = V_{sp}(s) - V_{fb}(s)$$
$$C(s) = V_{error}(s)\, G_c(s)$$

All these functions may be implemented using OP AMPs. Non-inverting and inverting OP AMP based implementations of the error amplifier are shown in Figure 4. A buffer amplifier should be used in the non-inverting configuration to isolate the thermistor circuit from R_{g1} unless $R_{g1} >> R_{therm}//R_o//R_{ref}$. A thermistor[3] with resistance, R_{therm} is used to sense temperature. Optionally, a resistor, R_o is added in parallel with the thermistor to linearize the thermistor response around the control temperature and also reduce the thermistor power dissipation. The value of R_o should be chosen to match the value of the thermistor at that temperature. Resistor R_{ref} is used to divide the reference voltage, V_{ref} and produce V_{therm}, the thermistor voltage. R_{ref} should be chosen large enough to limit the current through and the power dissipation in the thermistor to

avoid self-heating but small enough to allow enough voltage to be produced in response to temperature and thermistor resistance variations. It should also have a much lower temperature coefficient than the thermistor. V_{ref} must be a stable voltage so that V_{therm} is depended only on temperature variation. V_{ref} is also used to derive the set point voltage, V_{sp} and it is also imperative that the set point voltage is stable otherwise erratic behavior will result. Note that **the set point voltage should be set equal to the thermistor voltage at the desired control temperature**. This can be determined by calculating V_{therm} at that temperature.. The positions of the thermistor and R_{ref} should be swapped depending on whether a heater or thermoelectric cooler[4] (TEC) is the control element so that applied control is in the correct direction. The thermistor circuit output voltage will be $V_{therm} = V_{ref} [R_{therm} / (R_{ref} + R_{therm})]$ if the thermistor is connected to ground and $V_{therm} = V_{ref} [R_{ref} / (R_{ref} + R_{therm})]$ if the thermistor is connected to the reference voltage source. If R_o is used, substitute $R_{therm}//R_o$ for R_{therm}

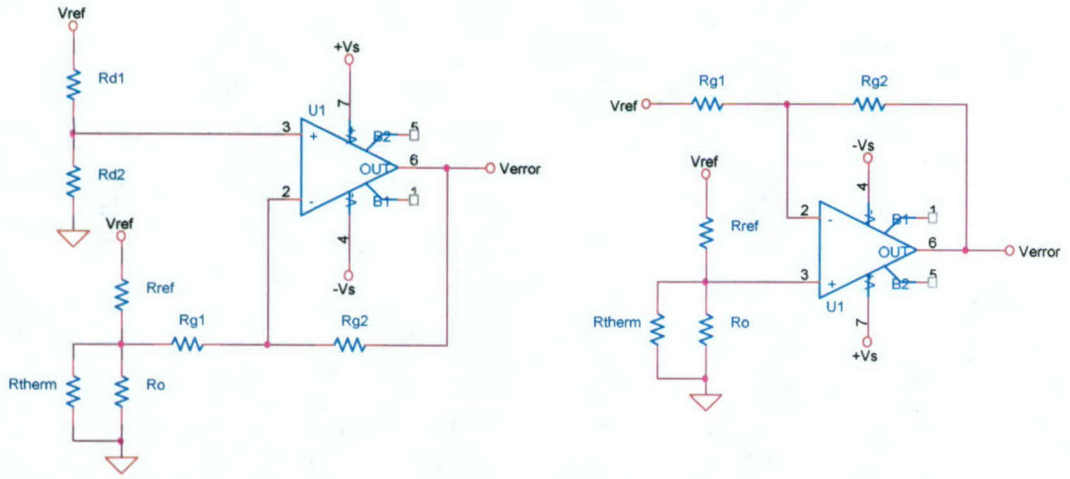

FIGURE 4. CIRCUITS OF NONINVERTING AND INVERTING ERROR AMPLIFIERS OF TEMPERATURE CONTROLLER.

The following relationships describe the function of the error amplifiers:

$$V_{error} = V_{sp} - V_{fb}$$

$$V_{therm} = V_{ref} (R_{therm)} / (R_{therm} + R_{ref})$$

Non-inverting:

$$V_{sp} = V_{ref} (R_{g2} / R_{g1} + 1) (R_{d2}) / (R_{d1} + R_{d2})$$

$$V_{fb} = V_{ref} (R_{g2} / R_{g1}) (R_{therm} / (R_{therm} + R_{ref})$$

Inverting:

$$V_{sp} = -V_{sref} (R_{g2} / R_{g1})$$

$$V_{fb} = -V_{ref} (R_{g2} / R_{g1} + 1) (R_{therm)} / (R_{therm} + R_{ref})$$

Figure 5 shows circuits of three different PID implementations based on OP AMPs. The top one uses four OP AMPs. One OP AMP is used to realize the proportional gain, a second to realize the integral gain, a third to realize the derivative gain, and a fourth to sum them together. The advantage of this circuit is that it allows setting the PID coefficients independently of each other. The disadvantage is that it requires four OP AMPS. Figure 5 also shows single OP AMP implementations of the PID function. One uses an inverting amplifier the other uses a non-inverting.

The relationships between component values and PID parameters for the above configurations are shown in the table of Figure 6. Needless to say PI control is much easier to design with single OP AMP configuration.

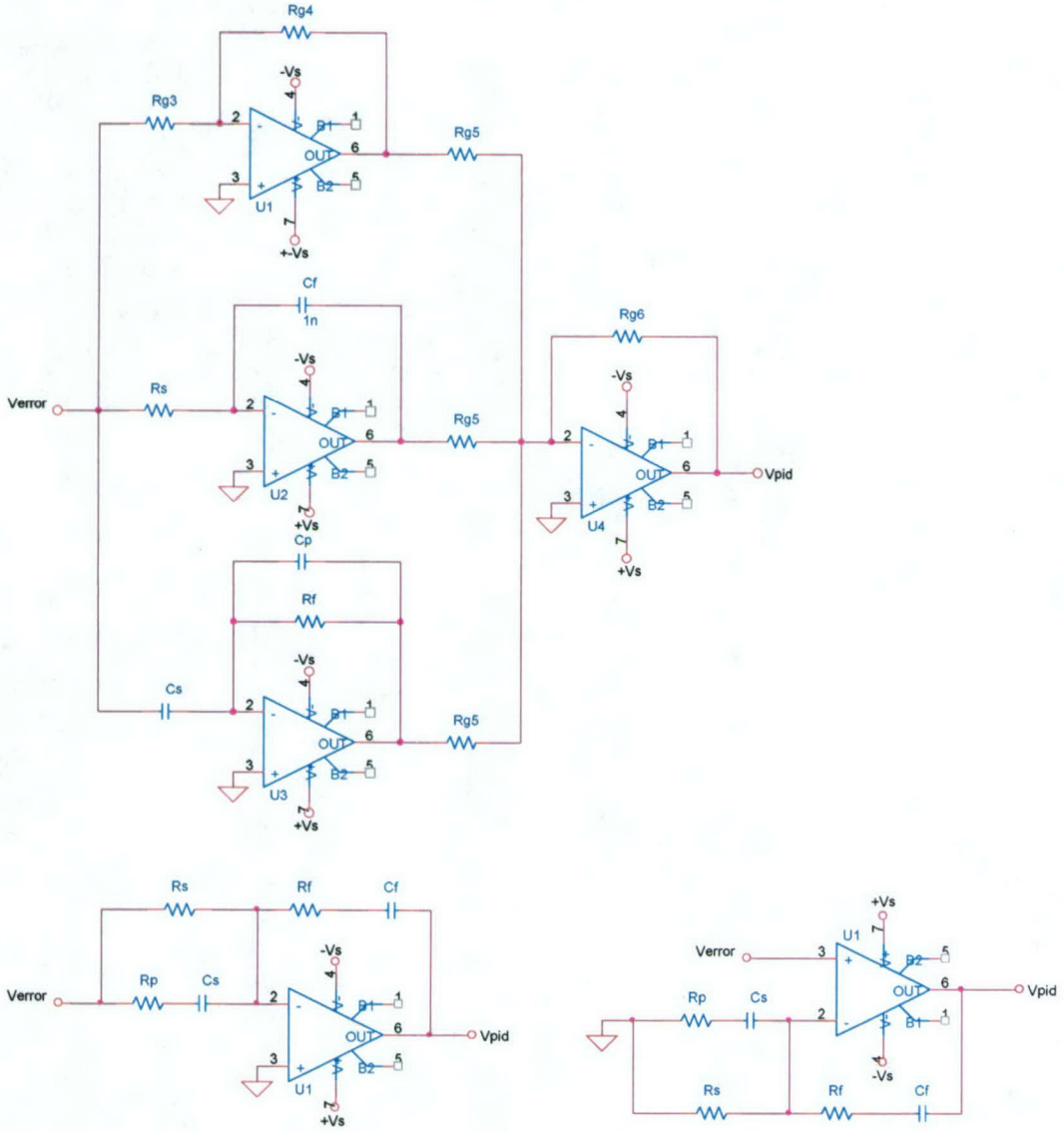

FIGURE 5. OP AMP PID IMPLEMENTATION

Four OP AMP PID implementation			
PID	PI	P	
$K_c = R_{g4} / R_{g3}$	$K_c = R_{g4} / R_{g3}$	$K_c = R_{g4} / R_{g3}$	
$\tau_I = R_s C_f$	$\tau_I = R_s C_f$		
$\tau_d = R_f C_s$			
Single OP AMP inverting PID implementation			
PID	PI	P	
$K_c = (R_p + R_s) C_s + R_f C_f) / R_s C_f = R_f / R_s$	$K_c = R_f / R_s$	$K_c = R_f / R_s$	$R_s >> R_p$ and $R_s C_s << R_f C_f$
$\tau_I = R_s C_f$	$\tau_I = R_s C_f$		
$\tau_d = (R_p + R_s) R_f C_s / R_s = R_f C_s$	No C_s, R_p	No C_s, R_p, C_f	
Single OP AMP non-inverting PID implementation			
PID	PI	P	
$K_c = (R_p + R_s) C_s + (R_f + R_s) C_f) / R_s C_f = R_f / R_s + 1$	$K_c = R_f / R_s + 1$	$K_c = R_f / R_s + 1$	$R_s >> R_p$ and $R_s C_s << R_f C_f$
$\tau_I = R_s C_f$	$\tau_I = R_s C_f$		
$\tau_d = (2R_p + R_s) R_f C_s / R_s = R_f C_s$ for $R_s >> R_p$	No C_s, R_p	No C_s, R_p, C_f	

FIGURE 6. TABLE OF PID DESIGN RELATIONS

In the four OP AMP implementation, capacitor C_p of the differentiator together with R_f provide a roll-off that causes the derivative part of the response to level off and preserve amplifier stability. The roll-off frequency should be chosen high enough so that it does not interfere with PID control but low enough to avoid instability considering the OP AMP open loop gain. Capacitor C_p and resistor R_s, in the single OP AMP implementation, perform a similar function.

The circuit of a bipolar driver for a thermoelectric cooler[3], TEC is shown in Figure 7. It is based on a transconductance amplifier (voltage to current converter) configuration with Darlington power transistors, Q_1 and Q_3, at the output of the OP AMP acting as current boosters (darling tons are necessary to avoid overloading the OP AMP as TEC present very low resistance. If unipolar operation is called for, one of the transistors can be eliminated. Transistors Q_2 and Q_4 together with resistors R_{sc} limit the current to V_{BE}/R_{sc}. Alternatively the output swing of the OP AMP stage can be adjusted via the supply voltages +Vs/-Vs to limit the load current. Resistor R_c, converts the input voltage to TEC current and should be chosen as low as possible to avoid unnecessary power consumption. For the same reason, power supply voltages $+V_c$ and $-V_c$ should be chosen to cover only the voltage drops in R_c, TEC, and collector to emitter.

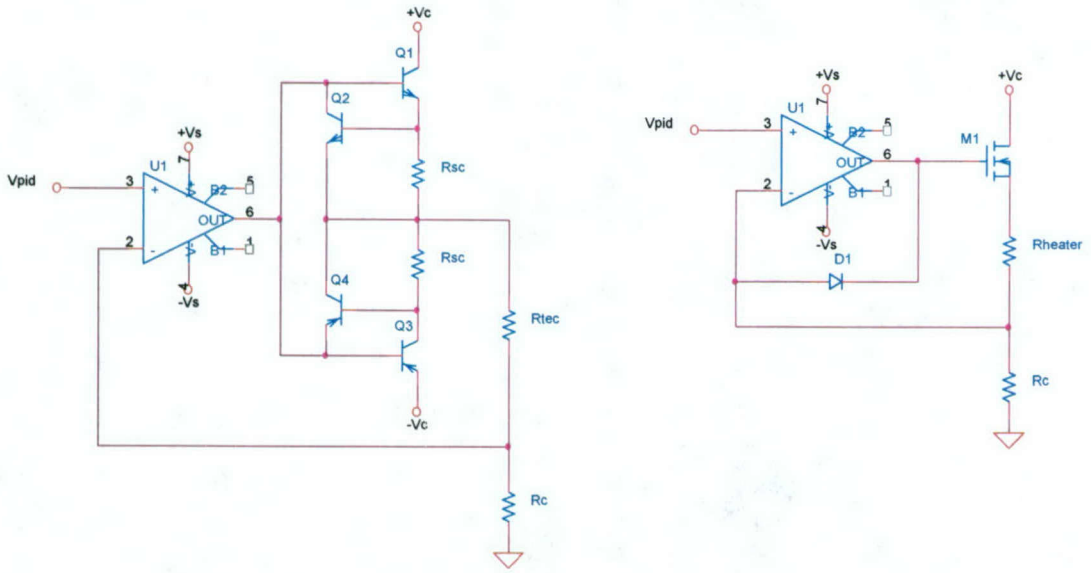

FIGURE 7. CIRCUIT OF A TEC DRIVER OF TEMPERATURE CONTROLLER AND OF A HEATER DRIVER.

The following relationships apply to a TEC driver:

$$I_{tec} = V_{pid} / R_c$$

$$P_{tec} \sim I_{tec}^2 R_{tec}$$

$$P_Q = +V_c - (R_{sc} + R_{tec}) I_{tec} - V_{pid}$$

The second circuit shown in Figure 6 drives a heater. It utilizes a power MOSFET. A power MOSFET outperforms the bipolar in this application. Taking advantage of its low on resistance results in reduced total power dissipation and lower $+V_c$. A complimentary power MOSFETs could have been used instead of bipolars in the TEC cooler driver. In addition, it provides an extremely high input resistance independent of load. The following relationships apply to a heater driver:

$$I_{heater} = V_{pid} / R_c$$

$$P_{heater} = I_{heater}^2 R_{heater}$$

$$P_Q = +V_c - R_{heater} I_{heater} - V_{pid}$$

In either case the maximum power dissipated by the transistor is given by (see appendix):

$$P_{Q\,max} = \tfrac{3}{4} V_c^2 / R \text{ and occurs at load current}$$

$I_L = V_c / 2\,R$ where R is the sum of all resistances in the load current path.

Two alternate drivers are shown in Figure 8. The one on the left is voltage amplifier not transconductance. The one on the right is a transconductance amplifier with the load connected to the drain (inverting).

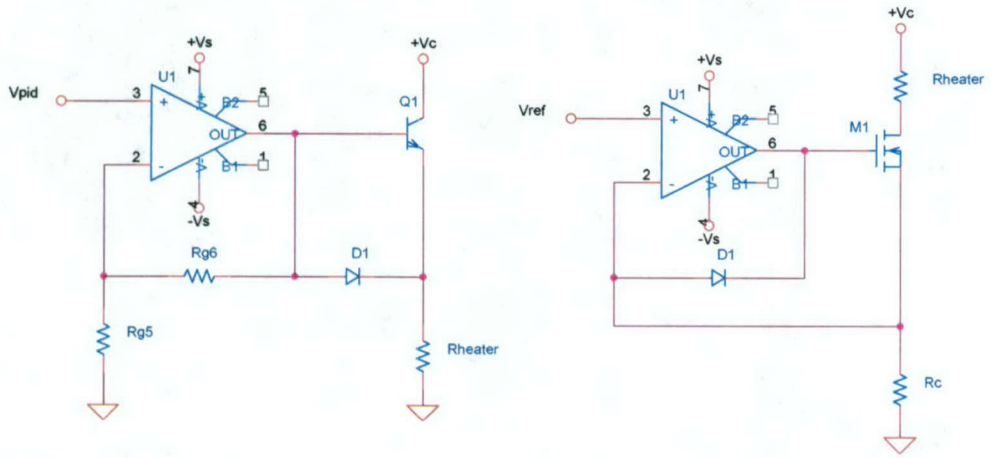

FIGURE 8. ALTERNATE DRIVERS.

Overall a controller designed with the above components will require three to six OP AMPS to realize. It is possible however to implement a controller using a single OP AMP as shown in Figure 9. It can be analyzed and the transfer function be derived by considering the Thevenin equivalent circuits of the two networks connected to the OP AMP inputs[5]. The penalty for reduced hardware lies in the complexity of the design calculations as there is loading between components. It can be simplified, however, if derivative control is not necessary, by eliminating capacitor C_s. The OP AMP should have low input offset voltage drift and bias current drift, as drifts with temperature of these quantities will have the same effect as set point drifts.

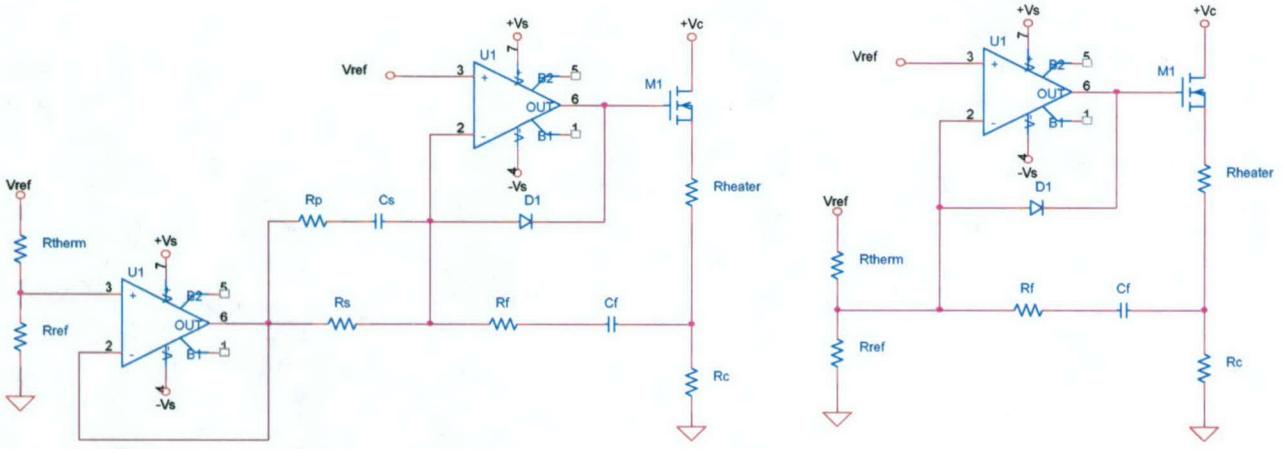

FIGURE 9. COMBINATION TEMPERATURE CONTROLLERS

The single non-inverting OP AMP PID relations apply in this case too. In the second circuit $R_s = R_{ref} // R_{therm} // R_o$ and capacitor C_p together with R_s provides a high frequency roll-off for stability.

Digital Control Implementation

Digital control refers to control implementations that either utilize digital hardware or software code in embedded processors. We will concentrate on the latter here. Digital control systems[6,7] can be based on analog counterparts by

discretizing the transfer function using the z transform. A/D and D/A converters are commonly used to discretize the contolled signals or sometimes are directly inputted to or outputted from the processor. For example some processors have built in interfaces that can read frequency (pulses) directly and output a pulse width modulated signal.

A block diagram of a digital control system is shown in Figure 10. The only analog part is the plant.

To discretize the controller transfer function, I recommend using the Tustin or bilinear transform $s \leftarrow (2 / T_s)(1 - z^{-1}) / (1 + z^{-1})$ proposed by Irfan[8], which is the most stable and in my experience works best for the controller. This can be done as follows:

$$G_c(z) = K_c (1 + 1/s\tau_i + s\tau_d) \mid_{s = (Ts/2)(1 - z\text{-}1 / 1 + z\text{-}1)}$$
$$= [b_o + b_1 z^{-1} + b_2 z^{-2}] / [a_0 + a_1 z^{-1} + a_2 z^{-2}]$$

Where $b_o = K_c(\alpha + \beta + 1)$, $b_1 = K_c(2\alpha - 2\beta)$, $b_2 = K_c(\alpha + \beta - 1)$, $a_0 = 1$, $a_2 = 0$, $a_2 = -1$ and $\alpha = T_s / 2\tau_i$, $\beta = 2\tau_d / T_s$. T_s is the sampling period of the system. Note that z^{-1} represents a delay of one sampling period and z^{-2} represents a delay of two sampling periods. In recursive difference equation form this will be:

$$C(n) = b_0 T_e(n) + b_1 T_e(n-1) + b_2 T_e(n-1) - a_2 C(n-2).$$

To complete the loop we need a relationship between error and set point, hence

$$T_e(n) = T_{sp}(n) - T_o(n-1).$$

Hence the processor computes the control output C(n) based on data acquisition of the output $T_o(n)$ and computation of the error signal $T_e(n)$.

For successful implementation and control the sampling period must be much smaller than the controller time constants. So $T_s < \tau_I / 10$ and $T_s < \tau_d / 10$. The bit resolution of the D/A need be $m > -\log_2(K_c T_s / \tau_i)$ to avoid integration round off error.

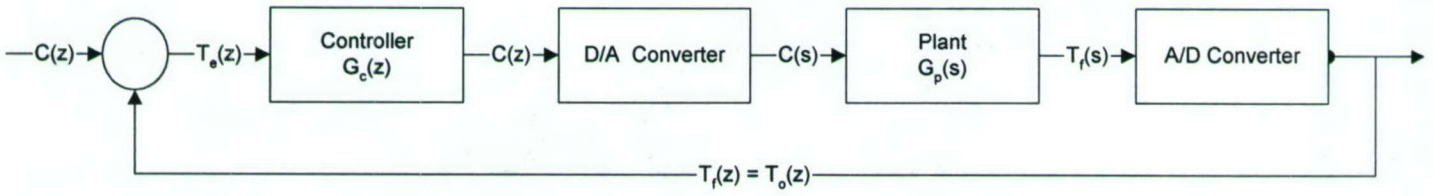

FIGURE 10. BLOCK DIAGRAM OF A DIGITAL CONTROL SYSTEM

An alternative implementation of a digital controller proposed by Astrom[9] offers limiting proportional control action to a percentage of the set point, leveling off the derivative action while limiting it to changes of output only, and unwinding the integrator at the expense of additional computation is described below. Note that backward difference $s \leftarrow (1 - z^{-1}) / T_s$ transform is used.

$$C_s(n) = C_i(n) + C_p(n) + C_d(n)$$

$$C(n) = \begin{cases} C_{max} & \text{if } C_s(n) > C_{max} \\ C_s(n) & \text{if } C_{min} \le C_s(n) \le C_{max} \\ C_{max} & \text{if } C_s(n) < C_{min} \end{cases}$$

$$C_p(n) = a_c [bT_{sp}(n) - T_f(n)]$$
$$C_d(n) = a_d C_d(n-1) + b_d [T_f(n-1) - T_f(n-2)]$$
$$C_i(n) = C_i(n-1) + b_i [T_{sp}(n-1) - T_f(n)] + b_t [C_s(n) - C(n)]$$

Where $a_c = K_c$, $a_d = \tau_d / (\tau_d + NT_s)$, $b_d = K_c \tau_d / (\tau_d + NT_s)$, $b_i = K_c T_s / \tau_i$, $b_t = K_c T_s / \tau_t$, $b \le 1$, $\tau_t \sim \tau_d$, $N = 5 - 20$. For best results the sampling period should be $0.1 \tau_I < T_s < 0.3 \tau_I$ for PI control and $0.2 \tau_d / N < T_s < 0.6 \tau_d / N$ for PID control.

For computer simulations, the plant can be descretized using the impulse invariant z transform, which in my experience gives the best results for plant modeling as follows:

$$G_p(z) = \mathcal{Z}\{K_p (1 - sT_d/2) / [(1 + sT_d/2)(sT_r + 1)]\}$$

$$= \mathcal{Z}\{A_1 / (s + 2/T_d) + A_2 / (s + 1/T_r)\} \text{ by partial fraction expansion}$$

$$= A_1 / (1 - \alpha z^{-1}) + A_2 / (1 - \beta z^{-1})\} \text{ from z transform tables}$$

$$= [b_0 + b_1 z^{-1}] / [a_0 + a_1 z^{-1} + a_2 z^{-2}]$$

Where $b_0 = A_1 + A_2$, $b1 = -(\beta A_1 + \alpha A_2)$, $a0 = 1$, $a_1 = -(\alpha + \beta)$, $a_2 = \alpha \beta$ and

$A_1 = 4K_p / (T_d - 2T_r)$, $A_2 = (K_p / Tr) [(2T_r + T_d) / [(T_r - T_d)]$, $\alpha = e^{-2Ts/Td}$, $\beta = e^{-Ts/Tr}$

In recursive difference equation form this will be:

$$T_o(n) = b_o C(n) + b_1 C(n-1) - a_1 T_o(n-1) - a_2 T_o(n-2)$$

An interesting implementation of a controller (non PID) is the deadbeat controller. So called because it settles in $(n + 1)T_s$. Where n is the order of the plant $G_p(z)$

$$G_p(z) = [a_0 + a_1 z^{-1} + a_2 z^{-2} + \ldots + a_n z^{-n}] / [b_0 + b_1 z^{-1} + b_2 z^{-2} + \ldots + b_n z^{-n}]$$

The controller $G_c(z)$ must be the same order as the plant.

$$G_c(z) = [p_0 + p_1 z^{-1} + p_2 z^{-2} + \ldots + p_n z^{-n}] / [q_0 + q_1 z^{-1} + q_2 z^{-2} + \ldots + q_n z^{-n}]$$

If the coefficients are set as follows:

$$p_0 = r / (b_0 + b_1 + b_2 + b_n),\ q_0 = r - b_0 p_0$$

$$p_1 = a_1 p_0,\ q_1 = -b_1 p_0$$

$$p_2 = a_2 p_0,\ q_2 = -b_2 p_0$$

$$p_n = a_n p_0,\ q_n = -b_n p_0$$

All poles of the plant are cancelled and replaced by poles at the origin. This type of control system must be applied only to very stable systems with very short sampling periods that a large overshoot is acceptable.

Plant Identification and Controller Tuning

Plant identification implies estimation of the plant parameters K_p, T_r, and T_d. These can be determined by observing the plant input and output signals[10].

Controller tuning refers to optimally setting the controller parameters (or ζ and ω_n) based on plant parameters for the purpose of meeting specifications. Optimally means the best under the plant constrains which may or may not end up meeting specifications.

Case1: Open Loop

Use this method if the plant input is accessible.

1. Let the plant output settle.
2. Apply a step change to the input of the plant at time 0.
3. Record and plot the output signal (see the plot in Figure 11).
4. Determine the parameters $\Delta V = V_2 - V_1$, $\Delta T = T_2 - T_1$, T_d, and T_r as shown in the plot.
5. Calculate the control parameters using the relationships shown in the table of Figure 12.

A more accurate estimation of T_r is by plugging any pair of points $T_0(t_o)$, t_o in $T_0(t_o) = T1 + \Delta T (1 - e^{-to/Tr})$ and solving for T_r.

Hence $T_r = -t_o / \ln [1 - (T_0(t_o) - T1) / \Delta T]$.

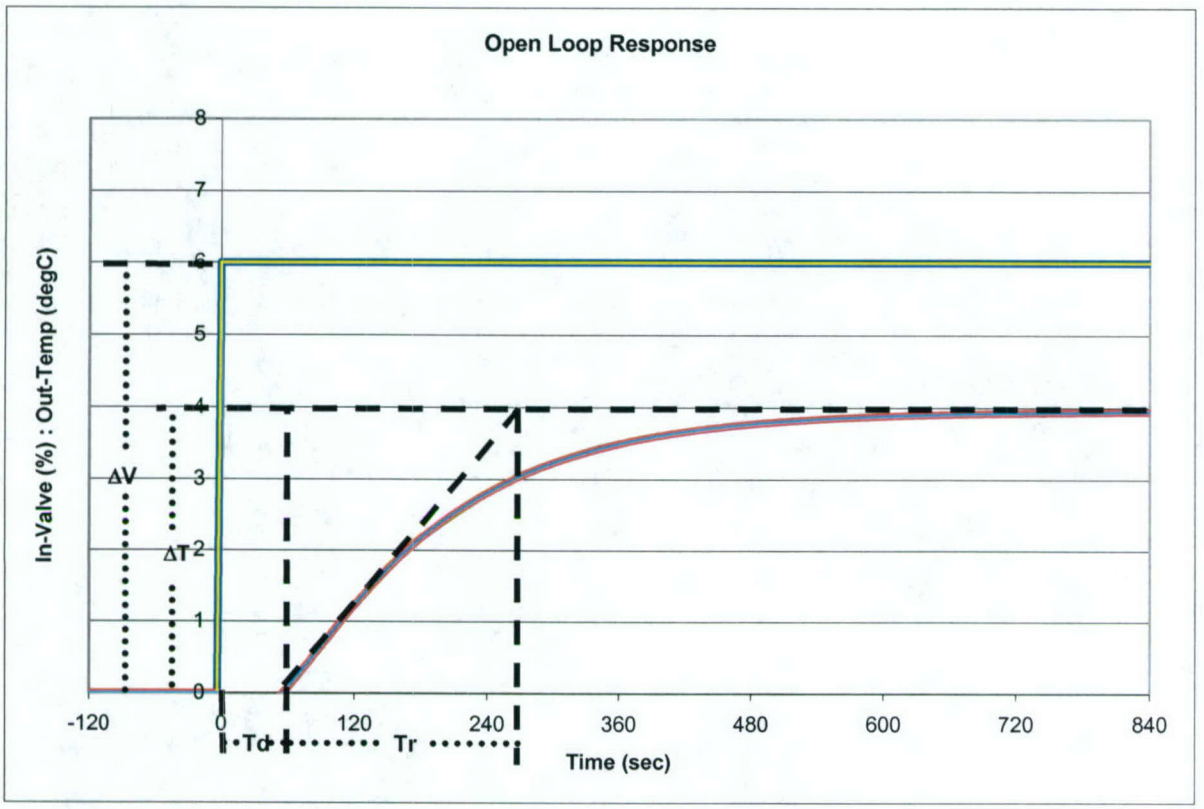

FIGURE 11. OPEN LOOP PLANT IDENTIFICATION

Controller	K_c	τ_i	τ_d
P	$T_r / (T_d K_p)$	-	-
PI	$0.9\ T_r / (T_d K_p)$	$3.3\ T_d$	-
PID	$1.2\ T_r / (T_d K_p)$	$2.0\ T_d$	$0.5\ T_d$

FIGURE 12. ZIEGLER-NICHOLS OPEN LOOP TUNING

If the plant output keeps increasing/decreasing with time, as shown in Figure 12, determine $\Delta V = V_2 - V_1$, $\Delta T = T_2 - T_1$, T_d, and T_r as shown in the plot of Figure 13.

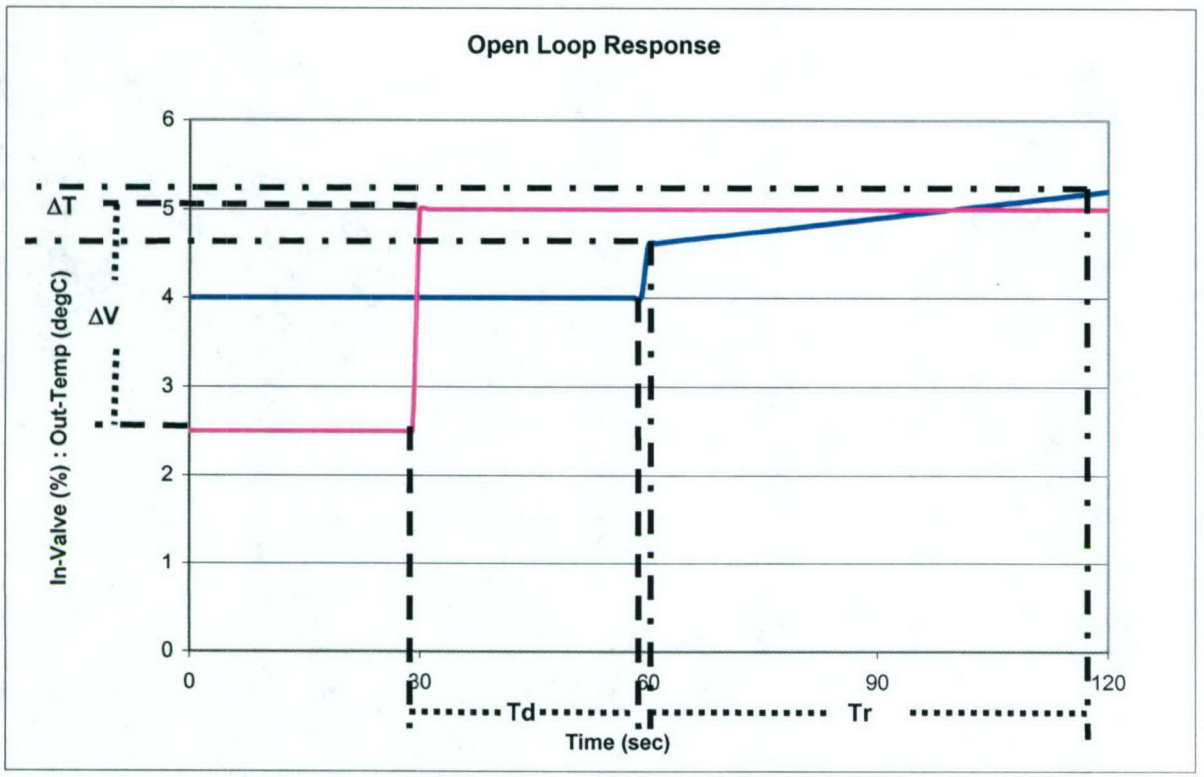

FIGURE 13. OPEN LOOP RESPONSE OFA NON REGULATING PROCESS

Case 2: Closed Loop

Closed loop methods are used if the plant input is not accessible.

1. Let the plant output settle.
2. Set the controller τ_i very large and τ_d very small to enable proportional control only. Then increase K_c until the output shows sustained oscillations.
3. Record and plot the output signal (see the plot in Figure 14).
4. Determine the parameter T_u ultimate period as shown in the plot and ultimate gain $K_u = K_c$ that causes oscillation.
5. Calculate the control parameters using the relationships shown in the table of Figure 15.

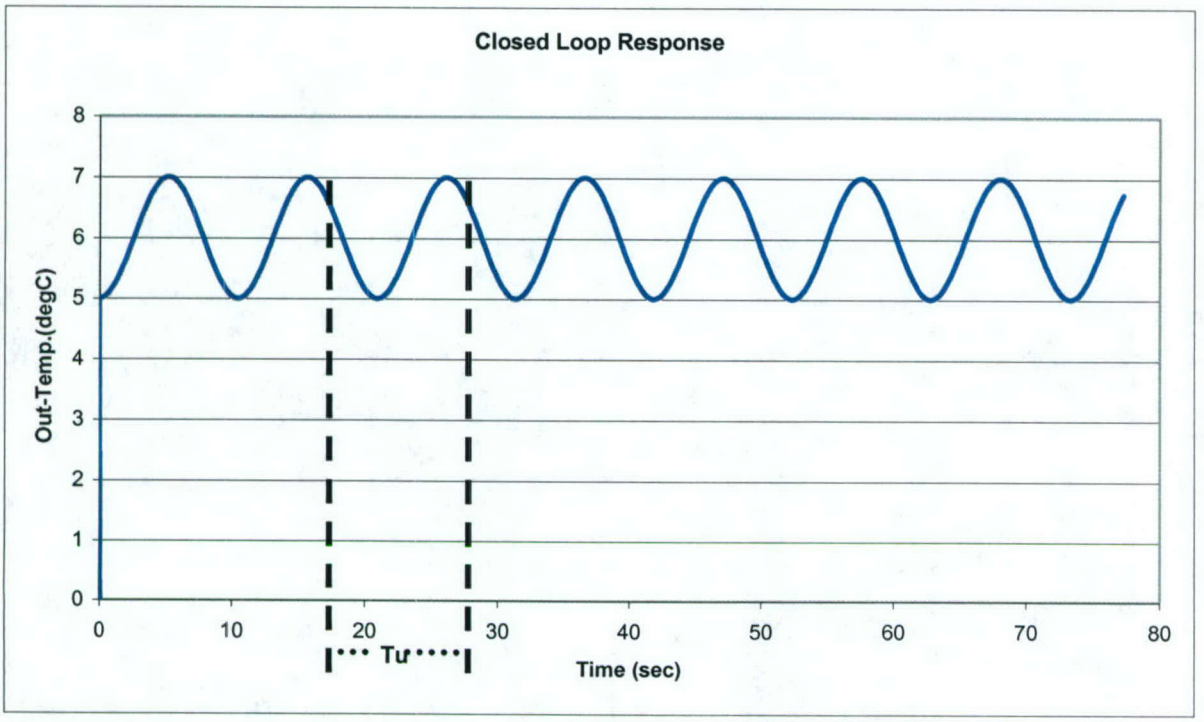

FIGURE 14. CLOSED LOOP PLANT IDENTIFICATION

Controller	K_c	τ_i	τ_d
P	0.50 K_u	-	-
PI	0.45 K_u	0.85 T_u	-
PID	0.60 K_u	0.50 T_u	0.125 T_u

FIGURE 15. ZIEGLER-NICHOLS CLOSED LOOP TUNING

Frequently it is too time consuming or unacceptable to force the plant to oscillate. An alternative method to the previous is to force the plant to damped oscillations and then approximate K_u and T_u.

1. Let the plant output settle.
2. Set the controller τ_i very large and τ_d very small to enable proportional control only. Then increase K_c until the output shows damped oscillations.
3. Record and plot the output signal (see the plot in Figure 16).
4. Determine parameters ΔT_1, ΔT_2, and Δt as shown in the plot.
5. Approximate the ultimate period as $T_u = 0.95\ \Delta t$ and the ultimate gain $K_u = K_c\ \Delta T_2 / \Delta T_1$.
6. Calculate the control parameters using the relationships shown in the table of Figure 15.

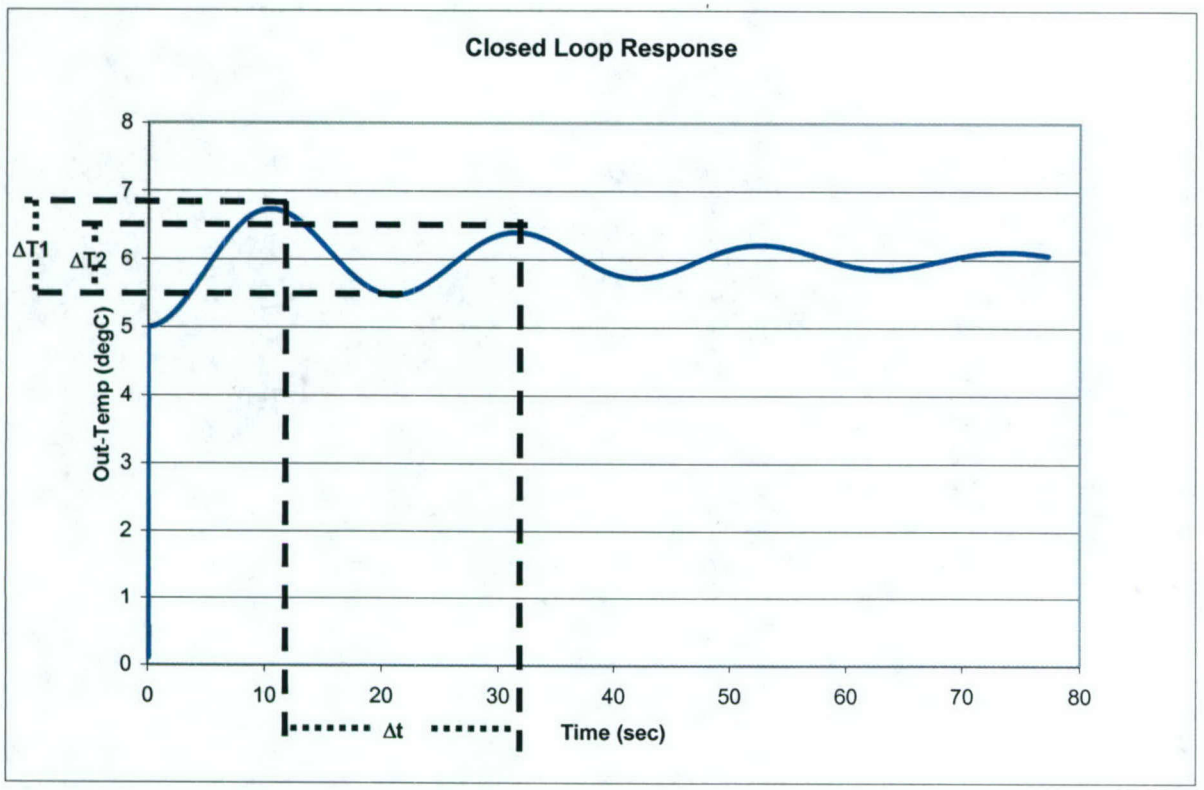

FIGURE 16. APPROXIMATE CLOSED LOOP PLANT IDENTIFICATION

Another closed loop method is the so-called relay method. In this approach the output is forced to oscillate by a small amount ΔT in response to oscillating input ΔV. This is accomplished by turning the controller to an ON/OFF type. That is Set the controller (without I and D control) such that when the error is positive it outputs a small fixed positive deviation from a fixed value V^+ and when the error is negative it outputs a small fixed negative deviation V^- ($\Delta V = V^+ - V^-$). This action will cause the plant to oscillate with amplitude ΔT. The exact shape of the oscillation will depend on its frequency and the plant roll offs. It may be nearly square, triangle, or sinusoid. A sinusoid will yield the best results as the amplitude of the first harmonic will be $|G_p(j2\pi/T_u)| = \Delta T = 4\,\Delta V / \pi K_u$. Then $K_u = 4\,\Delta V / \pi\,\Delta T$.

1. Let the plant output settle.
2. Set the controller to react as ON/OFF as explained.
3. Record and plot the output signal (see the plot in Figure 17).
4. Determine parameters ΔT and Δt as shown in the plot.
5. Then $T_u = \Delta t$ and the ultimate gain $K_u = 4\,\Delta V / \pi\,\Delta T$.
6. Calculate the control parameters using the relationships shown in the table of Figure 15.

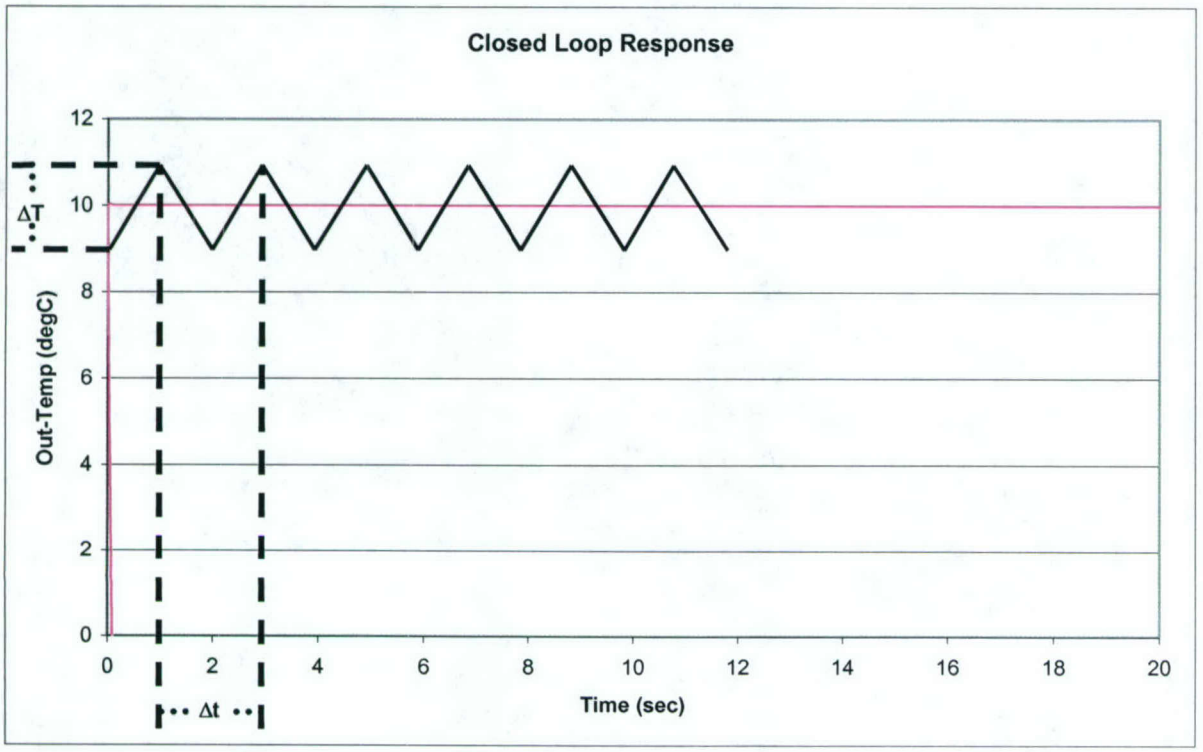

FIGURE 17. ALTERNATE CLOSED LOOP PLANT IDENTIFICATION

Case 3: Open or Closed Loop System ID

System identification methods can also be used to estimate the plant coefficients of its z-domain transfer function by autoregressive moving average (ARMA) least squares or other methods by operating on any set of plant input and output pairs. The analog plant parameters can be calculated from the z domain coefficients as follows.

$$T_d = -2T_s / \ln(\gamma),\ T_r = -T_s / \ln(\delta),\ K_p = -b_0\ T_r \text{ Where } \gamma = [a_1 +/- (a_1^2 + 4a_2)^{0.5}] / 2 \text{ and } \delta = -a_2 / \gamma$$

Other methods include frequency domain approach using FFT on the plant input and output signals to determine the plant transfer function.

Adaptive Control

Adaptive control[11,12] refers to ways of automatically adjusting the controller parameters based on plant identification in real time and while. This can be accomplished much easier with digital control. Ideally system identification methods can be applied in real time at any time to generate the controller coefficients. The deadbeat controller is ideal for adaptive control. However this approach requires matrix operations and is not suitable for small processors. There are several ways of implementing adaptive control but we will restrict this discussion to self-tuning or auto-tuning digital control.
Self-tuning refers to adjusting the controller parameters to the plant at start up. Auto-tuning refers to adjusting the controller parameters during operation in operation whenever it is practical to do so.

Theoretically any identification and tuning method can be applied for self-tuning or auto-tuning. However the simplest is to use the second or third closed loop method at times that it is possibly acceptable to disturb control, perhaps in the beginning of the process. A block diagram of self-tuning system is shown in Figure 18. The identifier looks at the plant input and output signals and determines the plant parameters. After that the converter calculates the controller coefficients using as input the plant parameters.

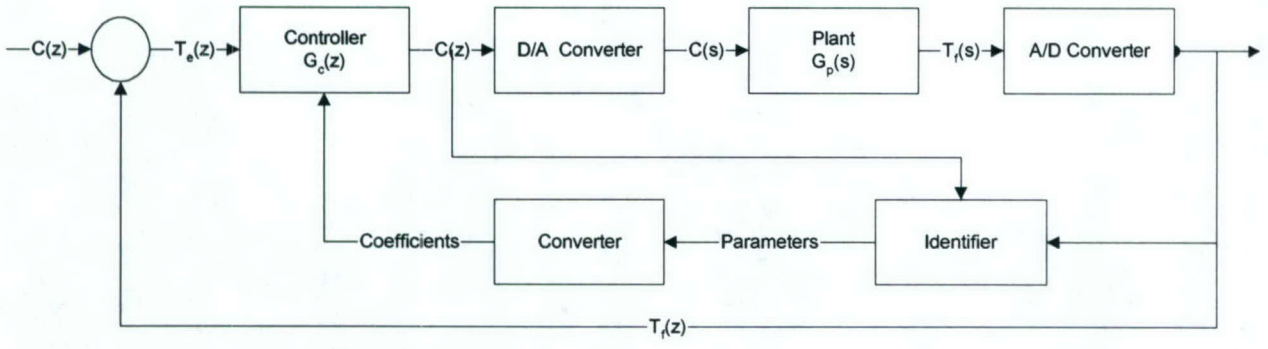

FIGURE 18. SELF TUNING CONTROLSYSTEM

The PID Transfer Function

The controller transfer function in frequency domain is given by.

$$G_c(j\omega) = K_c [\, 1 + j(\omega \tau_d - 1/\omega \tau_i)]$$

Its magnitude and phase are described by (see Fig. 19):

$$|G_c(j\omega)| = k_c ((1 + (\omega \tau_d - 1/\omega \tau_i)^2)^{1/2} \text{ and } \arg G_c(\omega) = \arctan [(\omega \tau_d - 1/\omega \tau_i)]$$

The magnitude of the transfer function in steady state can divided in frequency segments as follows:

$$|G_c(j\omega)| = \begin{cases} K_c \omega \tau_d & \text{for } \omega > \omega_o \\ K_c & \text{for } \omega = \omega_o \\ -K_c / \omega \tau_i & \text{for } \omega < \omega_o \end{cases}$$

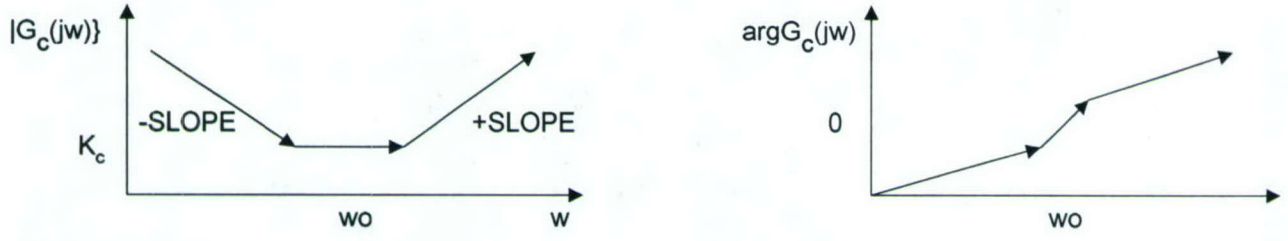

FIGURE 19. MAGITUDE AND PHASE PLOTS OF PID TRANSFER FUNCTION.

At frequency $\omega_o = 1/(\tau_i \tau_d)^{1/2}$, the magnitude will be $|H_{PID}(j\omega_o)| = k_c$, and the phase will be $\arg H(j\omega_o) = 0$.

For $\omega < \omega_o$ the slope of the magnitude will be -slope = $-k_c / \omega \tau_i$ while for $\omega > \omega_o$ +slope = $\omega k_c \tau_d$

Determination of PID parameters from Magnitude/Phase Plots

The PID parameters of an unknown controller can be determined by the magnitude and phase plots as follows:

- From phase plot, obtain ω_o (at zero phase).
- From magnitude plot, obtain k_c at ω_o and also get a pair k_1 at ω_1 and k_2 at ω_2 such that $\omega_2 > \omega_o > \omega_1$.
- Calculate $\tau_d = k_2 / \omega_2$, $\tau_i = 1/ k_1 \omega_1$

OP AMP PID Transfer Function Derivation

With reference to the single OP AMP PID implementations shown in Fig. 4 and Z_s being the source branch impedance and Z_f the feedback branch impedance the transfer functions are calculated as follows:

Inverting:

$$Z_s = \frac{R_s (s R_o C_s + 1) / s C_s}{R_s (s R_o C_s + 1) / (s (R_o + R_s) C_s + 1)}$$

$$Z_f / Z_s = \frac{(s R_f C_f + 1)(s (R_o + R_s) C_s + 1)}{(s R_s C_f)(s R_o C_s + 1)}$$

$$= \frac{s^2 (R_o + R_s) R_f C_s C_f + s((R_o + R_s) C_s + R_f C_f)) + 1}{s R_s C_f} \quad \frac{1}{s R_o C_s + 1}$$

Non-inverting:

$$Z_f / Z_s + 1 = \frac{s^2 (2R_o + R_s) R_f C_s C_f + s((R_o + R_s) C_s + (R_f + R_s) C_f) + 1}{s R_s C_f} \quad \frac{1}{s R_o C_s + 1}$$

Note: R_o results in a pole at $R_o C_s << 1/ \omega_o$ that is used to level off the derivative part of transfer function and preserve stability.

Transistor Driver Power Dissipation

The power dissipated in the transistor will be the product of the voltage drop across it, VQ (V_{CE} for bipolar and V_{DS} for MOSFET) times the load current through it:

$P_Q = V_Q I_L = V_c I_L - R I_L^2$ where $V_Q = V_c - R I_L$ and R is the sum of all resistances in the current path.

Taking the first two derivatives of the power with respect to load current we find:

$dP_Q/dI_L = V_c - 2 R I_L = 0 \rightarrow I_{L\,max} = V_c / 2 R$

$d^2P_Q/dI_L^2 = - 2 R I_L$. Therefore the maximum power dissipated by the transistor is

$P_{Q\,max} = ¾ V_c^2 / R$ at $I_L = V_c / 2 R$

The P_Q function is a curve, it is 0 at the origin and at V_c / R and peaks at $I_{L\,max}$.

Steinhart and Hart Equation

For quick reference, I include the equations that model a thermistor.

$1 / T = a + b \ln R + c (\ln R)^3$

a, b, and c can be solved for by measuring three (Ti, Ri) pairs and setting up a system of three linear equations.

$R = e^{\gamma}$

$\alpha = [a - (1/T)] / c$

$\beta = [(b / 3 c)^3 + \alpha^2 / 4]^{1/2}$

$\gamma = (\beta - \alpha / 2)^{1/3} - (\beta + \alpha / 2)^{1/3}$

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Introduction

While I was searching for applicable control approaches and methods, I was confronted with extensive information much of which is too theoretical, too practical, misleading, or simply not leading to a functional approach. Having spent a lot of time screening good and bad information, I decided to write this technical report and preserve my findings.

Purpose

The information I provide in this report is based on my own experience of approaches that work. I provide condensed information that is based on several texts and articles for the purpose of using it, at present and in the future, as a self contained reference.

Description of Apparatus and Setup

N/A.

Summary of Data and Results

To aid design and analysis of control systems, I created the following spreadsheets Calc_Tune PID.xls, Model_Control PID Irfan.xls and Model_Control PID Astrom.xls, Model_Therm YSI.xls. The first one does all the PID parameter calculations after entering the observation values as described in Plant Identification and Tuning. The second spreadsheet models a control system and plots inputs and outputs using Irfan approach while the third does the same using the Astrom approach. You may use them to determine best response that meets your specifications beyond the Ziegler-Nichols. The fourth spreadsheet models a standard YSI 400 thermistor. It will calculate the Steinhart-Hart coefficients for you around the specified temperature range. It will generate a table of points. It will plot the resistance-temperature curve. It will help you design a scaling amplifier to match the A/D input range. It will calculate and plot thermistor and amplifier output voltages. Finally it will help you do sensitivity and tolerance analysis. As an alternative analysis/design aid I created two OrCad PSpice programs, Model_Control PID Irfan.dsn and Model_Control PID Astrom.dsn to simulate the control system as alternatives to their EXCEL counterparts. The SPICE simulations are more realistic because they include signal limiters that I could not program in EXCEL.

Conclusions

N/A

Suggestions for Further Work

N/A

Appendix B

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00019

TITLE OF TECHNICAL REPORT		REVISION
Temperature Control of Mild-Moderate Hypothermia Induction Device		00
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-03	04/06/23
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Device Refinement	Mike Pitsakis	
TECHNICAL AREA		
Temperature Control		
SUBJECT AND KEY TECHNICAL WORDS		

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

TR_Hypo 030903 MP.doc

Abstract

Temperature data taken using the device built in utility that monitors and relays temperature and other information is reported here, comparisons are made, problems that were encountered are described together with solutions. Some data taken by SCRR staff at SCRR using the Mild-Moderate Engineering Prototype 1 on a live animal (pig) are also reported. The animal was cooled with respect to central core temperature from 38°C to 34°C at a flow rate of 200 mL/min in 6 minutes and was cooled from 34°C to 30°C at a flow rate of 500 mL/min in 2 minutes. Patient cooling time delays and cooling rates of Engineering Prototype 1 are faster than Engineering Prototype 2 in one measurement and about the same in another. Engineering Prototype 2 is a refined version with improved patient temperature stabilization. The design refinements described in the report should be used in the Clinical Prototype of this device.

Background

A previous technical report titled "Temperature Control Testing of the First Mild-Moderate Hypothermia Induction Device Prototype" (TR_Hypo 030903 MP.doc) on the subject of temperature control of Mild-Moderate Hypothermia Induction device, only described cooling rates and temperature stabilization of the cooling plates because at that time animal experiment data was not available and data using the "Pig Simulator" was not available because the device was not conceived yet. Since then we have taken plenty of data

Introduction

The first animal (pig) experiment data became available from SCRR in October of 2003 and showed that although patient cooling rates exceeded expectation, patient temperature stabilization was not optimized. Based on feedback from the SCRR we proceeded to refine the device as planned and optimized temperature control. Also in order to save animal lives, effort, and dollars, a device that would simulate an average sized pig in a thermodynamic sense for experiments at Ardiem Medical premises became a necessity. Such a device, named "Pig Simulator", was designed and constructed in November of 2003 and is described and characterized in technical report titled "Thermodynamic Simulator of a Pig" (TR_Hypo 031205 MP.doc).

Purpose

My aim in this report is to make temperature data available and describe the problems we encountered and the corresponding solutions.

Description of Apparatus and Setup

We designed the Mild-Moderate Hypothermia Induction device with the very important feature of outputting temperature and other data in real time (3 second update rate) over a serial link to a computer for saving and processing. Specifically the data includes a time stamp, device state (depends on function selected by user (normothermia, mild hypothermia, moderate hypothermia, or manual device control), flow rate, bypass valve % opening, heater % power, and the following temperatures: plate (controlled in mode 1), device internal air temperature, patient 1 (controlled in mode 3), patient 2 (auxiliary), outflow (from patient), and inflow (controlled in mode 2). The temperature is controlled by the discharge bypass valve (see diagram shown in Figure 1) and by the applied power to the heater. Both electrically controlled by embedded code. The heater is part of the evaporator. Figure 2 shows the cooling plates that comprise the evaporator part of the refrigeration system with a cooling bag inserted. The evaporator actually consists of a pair of top outer plates and a pair of bottom outer plates that sandwich the refrigerant tubing (coiled) and a pair of inner plates that sandwich the bag. The refrigerant tubing is inserted on the back side of the evaporator (not viewable). The plate temperature is monitored by a thermistor inserted in a hole on the top inner plate on the back of the evaporator.

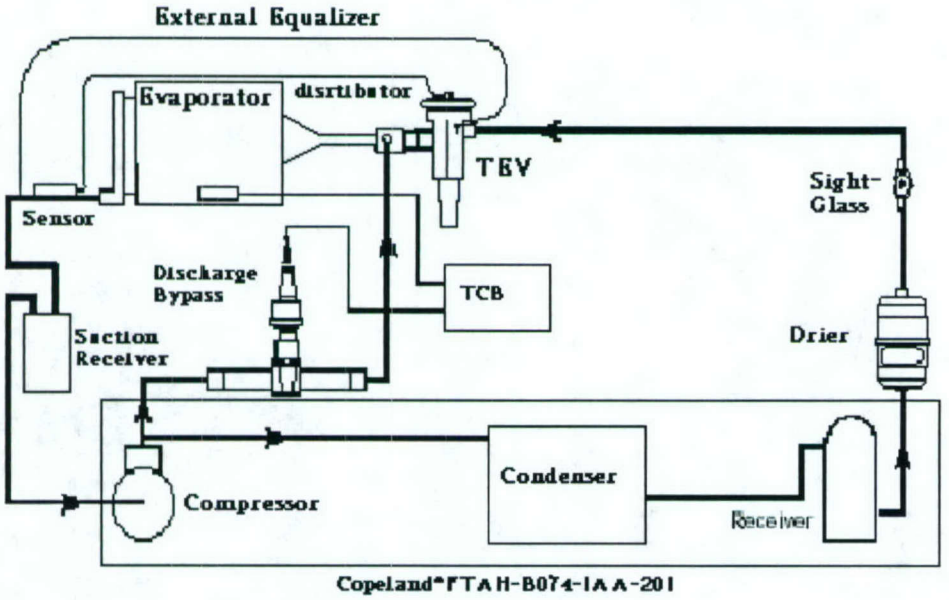


FIGURE 1

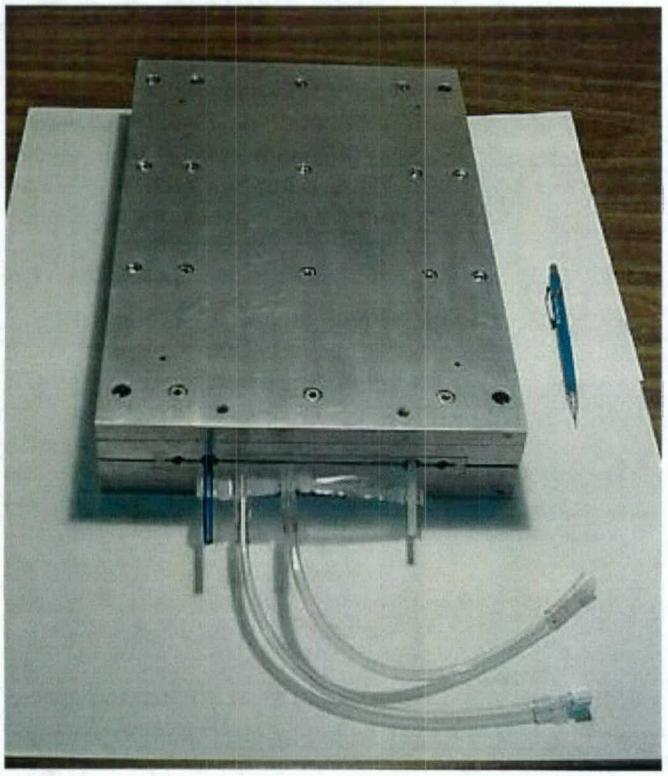


FIGURE 2

Engineering prototype 1, that was delivered to SCRR in August of 2003, contained a Copeland condensing units model FTAH-B074-IAA-201. This unit is specified as follows: current draw from the line 20.7 A maximum with an output of 2010 W at 7.2 °C evaporator and 32.2°C ambient. The original prototype had no heater installed. In December of 2003, we installed a heater and modified electronics and embedded code. The heater consisted of two 4" x 12", 120 VAC/240 W Kapton insulated foil heaters (0.011' thick) manufactured by Birk Manufacturing, Inc. One was placed on top of the top outer cooling plate and the other on top of the bottom outer cooling plate (total 480 W or 4 A). The arrangement did not provide enough heating power. Then we used a 2" x 12", 120 VAC/120 W Kapton insulated foil heaters (0.011' thick) manufactured by Birk Manufacturing, Inc on top and bottom left and on top and bottom right and on top middle plus a 4" x 12", 120 VAC/240 W (total 1080 W or 9 A). The heater power was controlled in an on/off fashion and the compressor was turned on/off in order to accomplish control. Note that because of power limitations (maximum current draw from the line[1] was set to 20 A in order to stay with what is typically available in a Hospital ER or OR), we were not able to have both compressor and heater on at the same time. This condition lead to clumsy control with over +/-1°C deviation from set-point (spec calls for +/-0.5°C see DRD) because the compressor was not meant for on/off operation. Turning the heater on/off is a nonlinear and not a very effective control approach, as is evident in the data plots shown in the next section. Also the heater power proved to be excessive.

Therefore we designed engineering prototype 2 with the following configuration:

a) A smaller compressor, Copeland condensing unit model M2FH-0056-IAA-201 which draws a maximum of 15.5 A from the line with an output of 1680 W at 7.2 °C evaporator and 32.2°C ambient.
b) Replaced the top and bottom outer plates by plates machined of low thermal conductivity plastic in order to reduce the mass of the evaporator and thus the time delays but also to provide some self insulation to heat absorbed from the environment.
c) First used, custom made for Ardiem Medical, 6" X 14", 120 VAC/480W Kapton insulated foil heaters (0.011' thick) manufactured by Birk Manufacturing, Inc. so that most surface area of the evaporator would be covered. One heater was sandwiched between the bottom outer plate and the top inner plate and the other was sandwiched between the top outer plate and the bottom inner plate. Unfortunately due to a defect the top heater burned by the lead attachment. However experiments conducted with one heater showed in extrapolation that the amount of heat that would be produced by two such heaters (total 960 W or 8 A) was still excessive. So we ordered and installed custom made heaters of the same size but of 360 W each (total 720 W or 6 A). Data taken is shown in the next section.

[1] See technical report titled "Current Draw of Hypothermia Induction Devices and Effect on Portability" (TR_Hypo 040622 MP.doc).

d) We designed and ordered a custom made bag 2" longer for increased efficiency which depends on surface area of bag contact to inner plates.

e) We used efficient temperature control algorithms described in technical report titled "Practical PID Feedback Temperature Control" (TR_Hypo 031125 MP.doc). The compressor was on continually while the discharge bypass valve was set at 20%, 30%, or 80% opening for stabilization at 30°C, 34°C, or 37°C respectively (these settings were found to result to 50% of the maximum power delivered to the heaters) while the heater power was controlled. During cooling, the heater power was set to 0. During warm up the valve was open 100%.

Summary of Data and Results

Data taken by SCRR staff at SCRR using Mild-Moderate Engineering Prototype 1 on a live animal (pig) are shown in Figure 3 and Figure 4. The animal was cooled with respect to central core temperature, Tcore from 38°C (normal for pigs) to 34°C at a flow rate of 200 mL/min in 6 minutes (Figure 1) and was cooled from 34°C to 30°C at a flow rate of 500 mL/min in 2 minutes. Other temperatures recorded are rectal, Trec and esophageal, Teso. Both of these are lagging central core temperature.

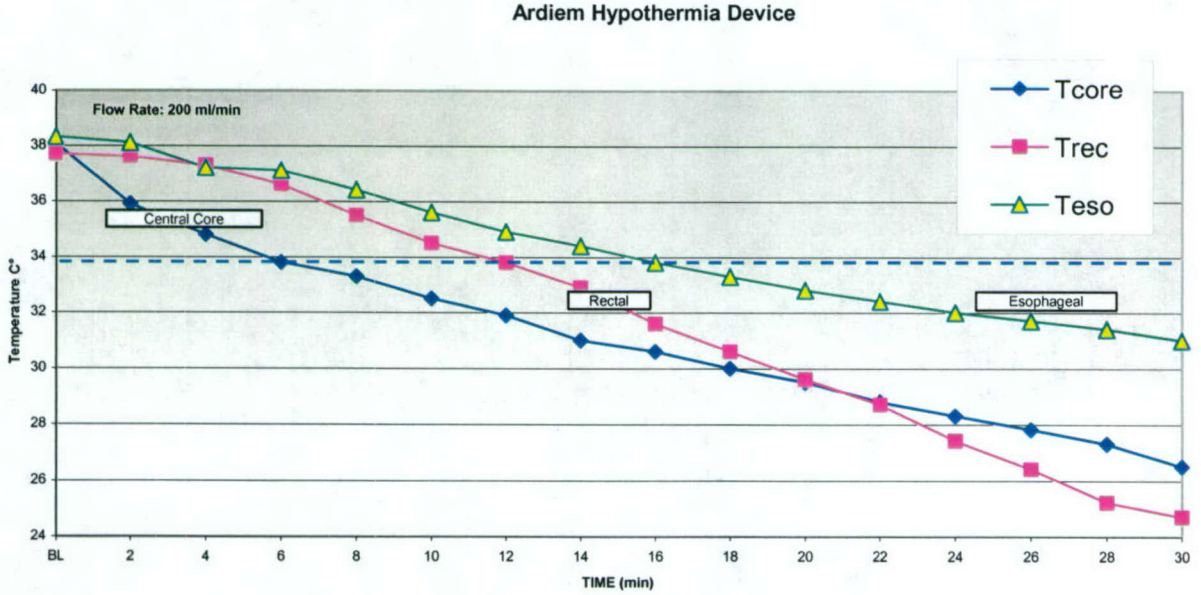


FIGURE 3

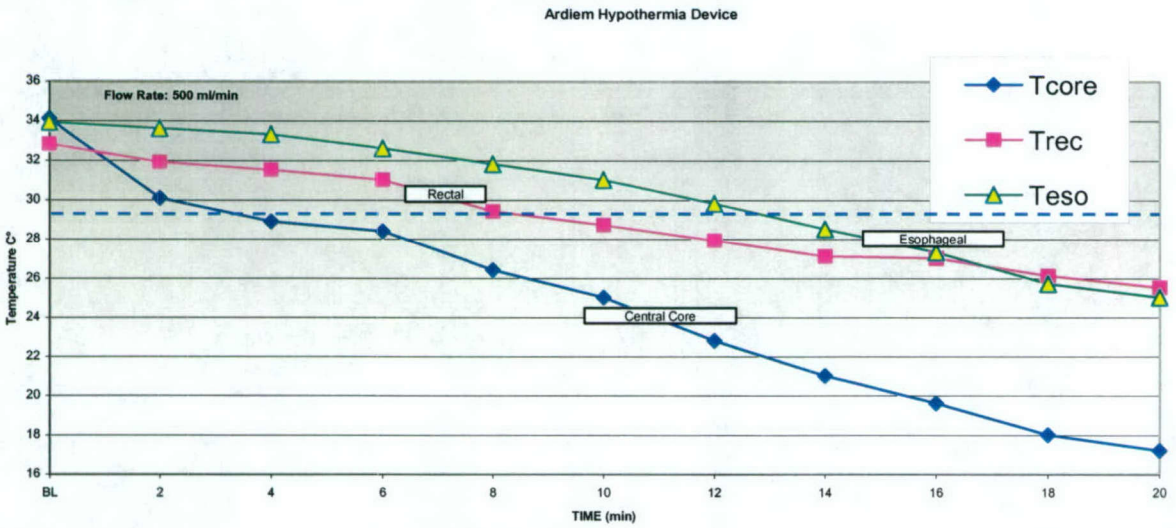


FIGURE 4

Plots of temperature taken by the device during the same experiment are shown in Figure 5 and Figure 6 below. The patient temperature was monitored by a probe inserted in the abdomen of the animal. In both plots, this temperature also lags the central core temperature. Outflow temperature is lower than patient temperature and shows a steady decline as expected. Inflow temperature is controlled at 6°C which is deemed cold enough but safe for the patient except for the initial drop due to the plate temperature being too low (Figure 5). This problem has been resolved. The system attempted to control outflow temperature to 6°C but the animal temperature was reduced to target before reaching it. Observe that the difference between plate and inflow temperatures increases as the flow rate increases which is also to be expected.

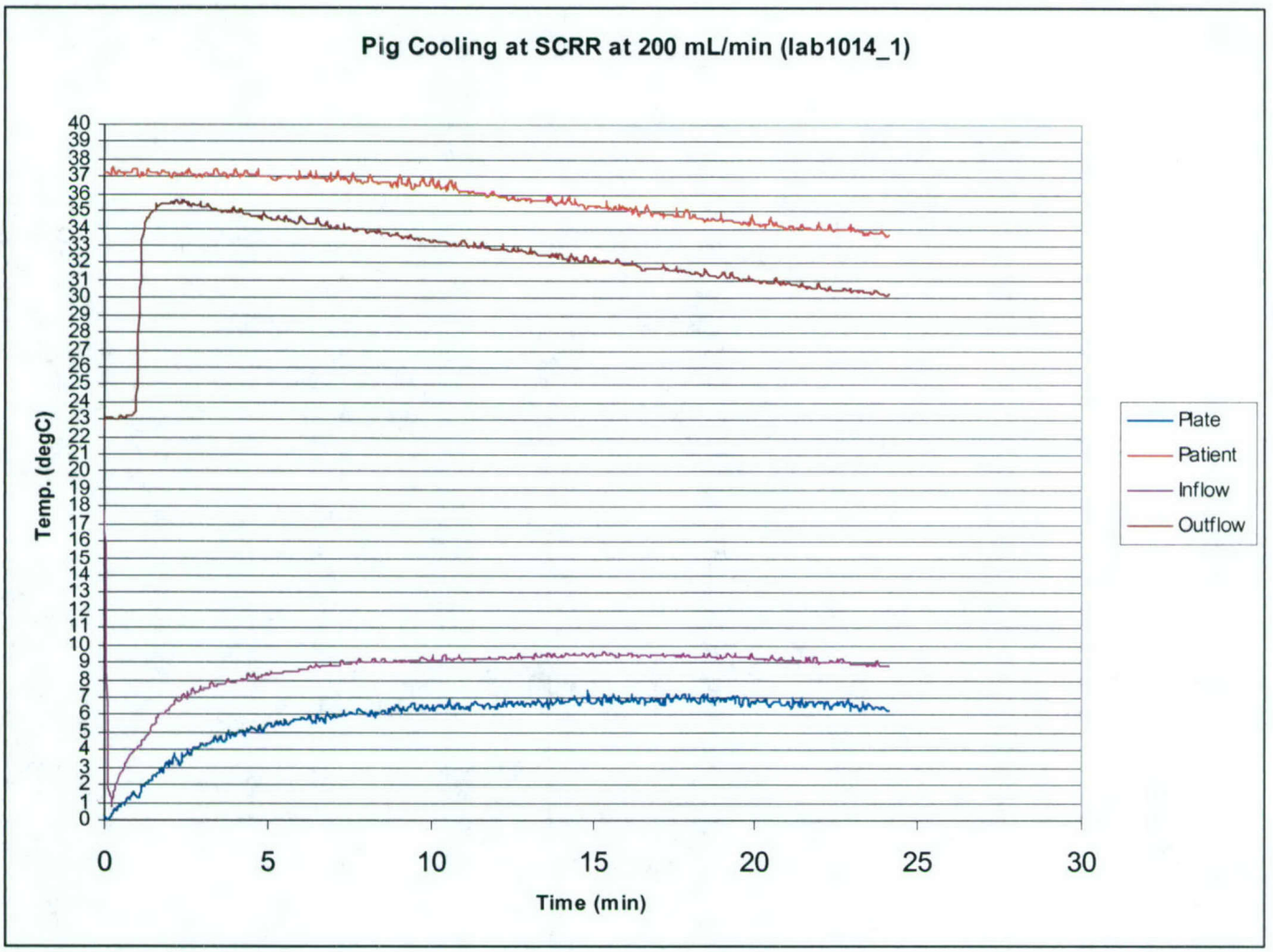


FIGURE 5

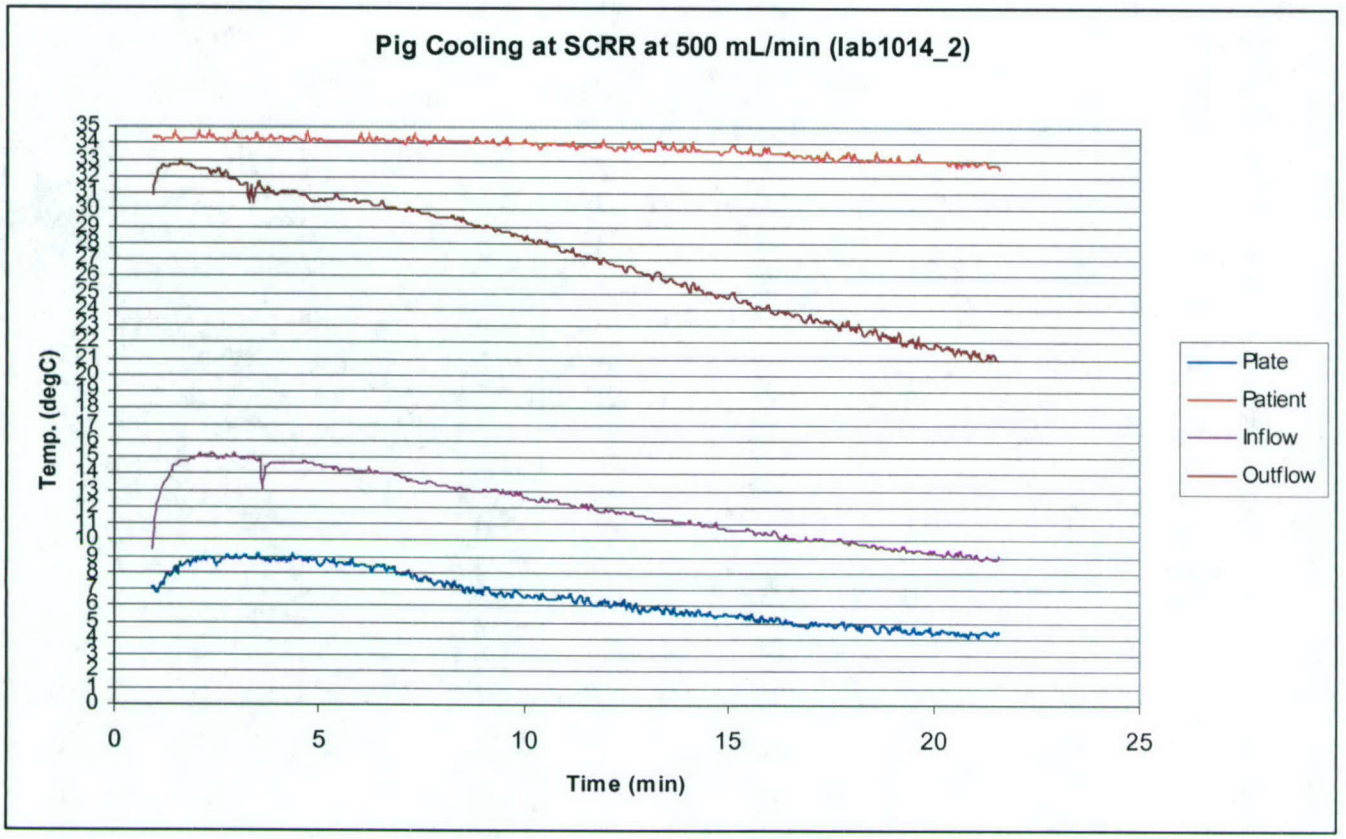


FIGURE 6

The plot in Figure 7 shows plate temperature versus time for one heater and two heaters. Heat is distributed evenly with two heaters (one on top and one on bottom) plus the response is much faster with two.

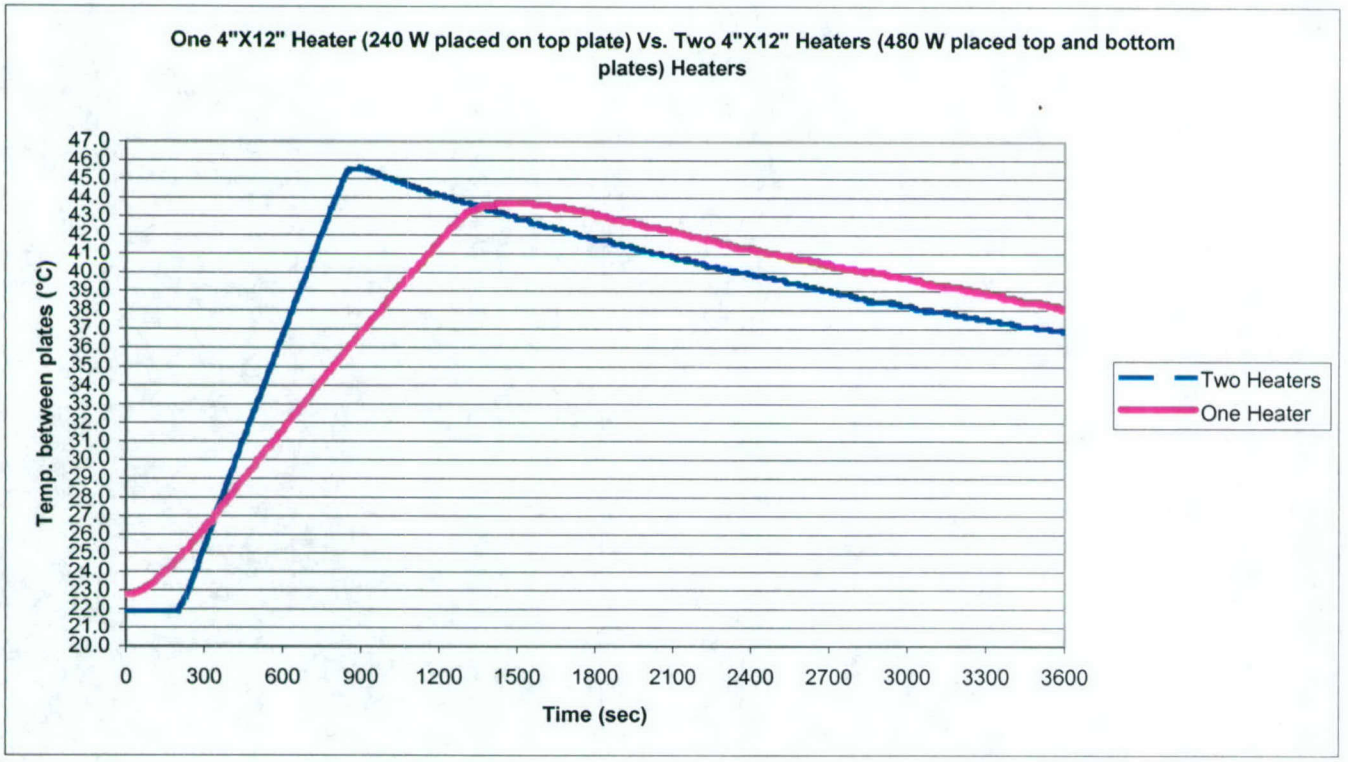


FIGURE 7

A plot of temperature data taken using Engineering Prototype 1 with 1080 W heaters as described in the previous section and using the "Pig Simulator" is shown in Figure 8. The experiment involved cooling the "Pig Simulator" from 38°C to 34°C and maintain at 34°C. Observe the large deviations of the inflow and plate temperatures and the effect on the controlled patient temperature.

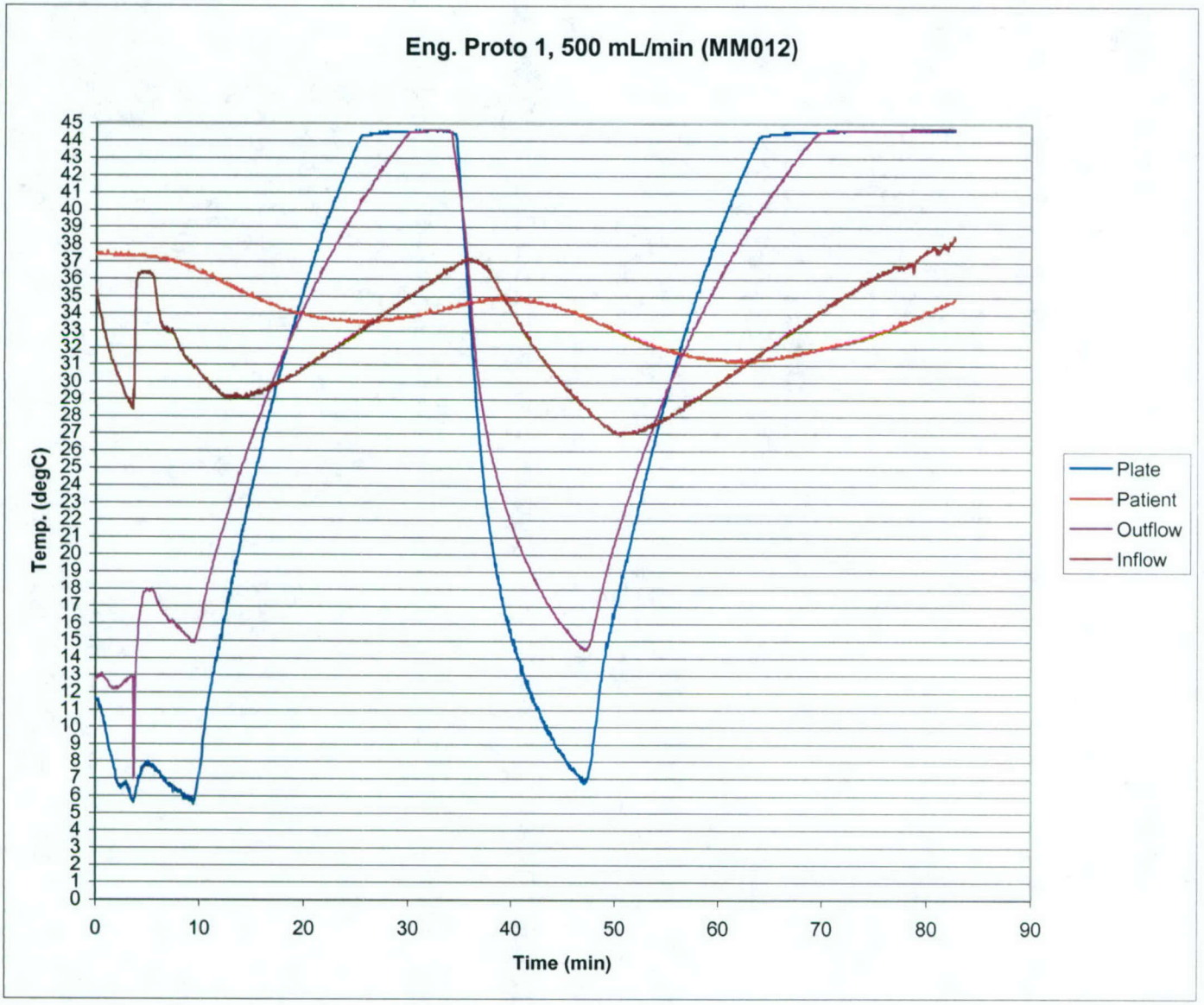


FIGURE 8

A plot of temperature data taken using the improved Engineering Prototype 2 with 720 W heaters as described in the previous section and using the "Pig Simulator" is shown in Figure 9. The experiment involved cooling the "Pig Simulator" to 30°C and maintain the temperature at 30°C. Observe the deviations of the inflow and plate temperatures are much smaller as inflow is controlled to 10°C (during cooling) for safety (limited by condensing unit). Also observe that the patient temperature is much tighter, +/-0.5°C as is controlled to the set-point (during stabilization).

A similar experiment was performed but the aim was to warm up the "Pig Simulator" to normal 37°C. A plot of temperature data taken is shown in Figure 10. Again observe the inflow and plate temperature deviations are much smaller as inflow is controlled to 44°C (during warm up) for safety and the patient temperature is much tighter +/-0.5°C as is controlled to the set-point (during stabilization).

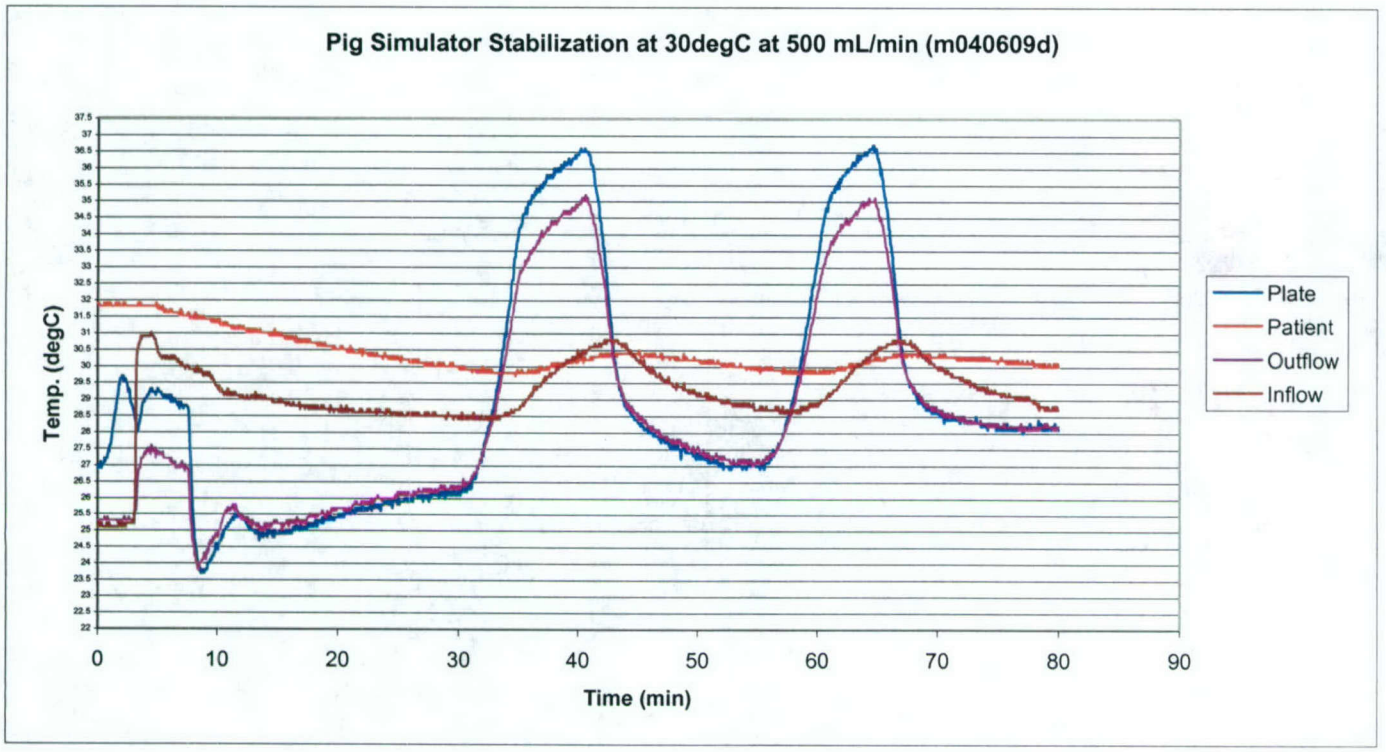


FIGURE 9

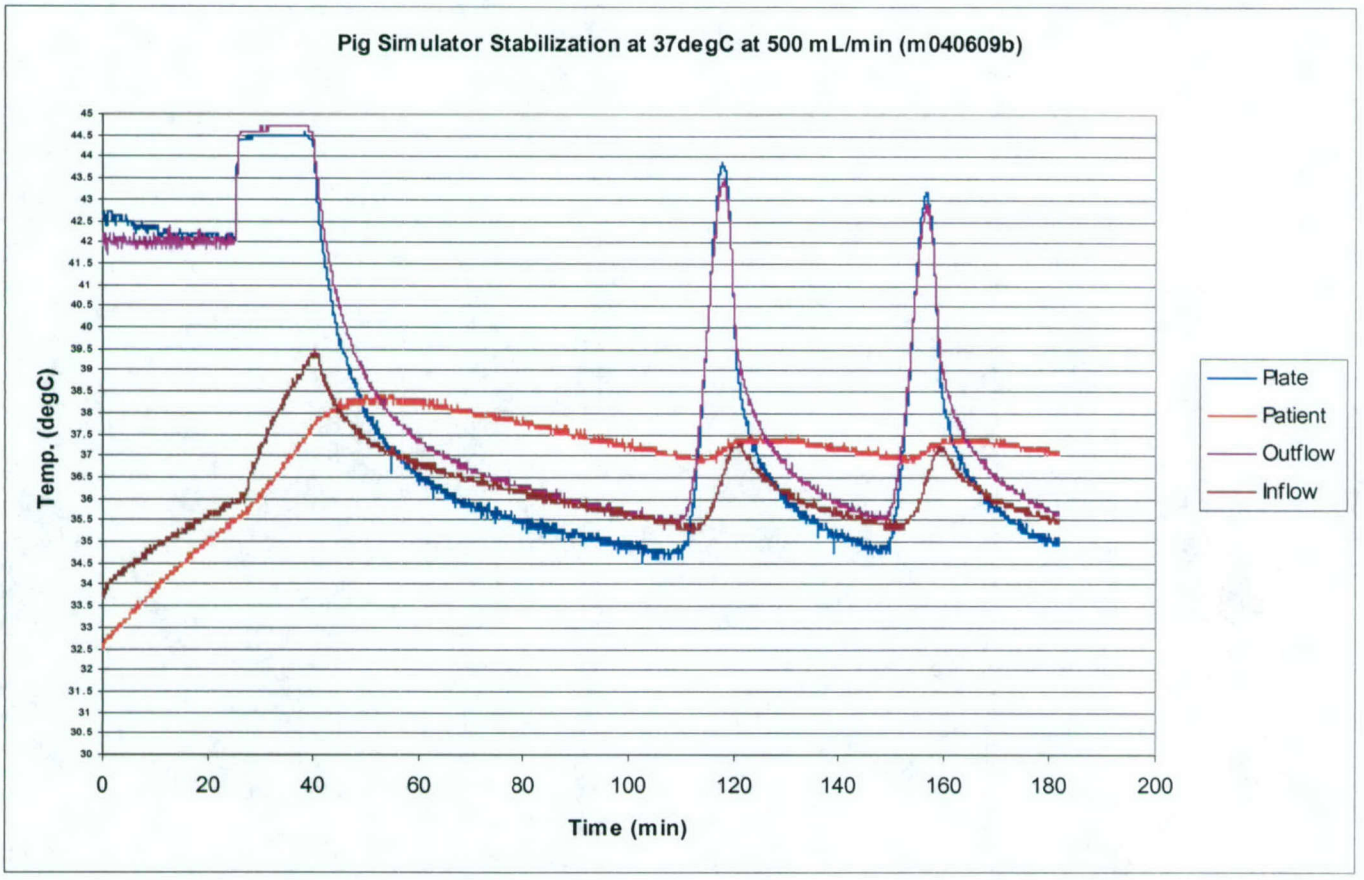


FIGURE 10

Further measurements and experimentation were carried to determine the effect of using long versus short bags, time delays and cooling rates between Engineering Prototype 1 and Prototype 2, and the effect of insulating the evaporator in Engineering Prototype 2. The resulting data are summarized in the table shown in Figure 11.

Eng. Prototype 1 w/ long bag and insulated evaporator

Flow rate (mL/min)	Cooling Delay (min)	Cooling Rate (degC/min)	Heating Delay (min)	Heating Rate (degC/min)	Data file name
200	11.550	0.165	8.950	0.189	CP2101-18/16
500	3.200	0.326	8.550	0.387	CP2101-9
900	2.000	0.443	5.000	0.390	CP2101-15

Eng. Prototype 2 w/ long bag and non-insulated evaporator

Flow rate (mL/min)	Cooling Delay (min)	Cooling Rate (degC/min)	Heating Delay (min)	Heating Rate (degC/min)	Data file name
200	2.850	0.132	9.000	0.165	CP2101-6
500	2.500	0.197	6.300	0.190	CP2101-12
900	1.450	0.246	5.050	0.209	CP2101-13

Eng. Prototype 2 w/ long bag and insulated evaporator

Flow rate (mL/min)	Cooling Delay (min)	Cooling Rate (degC/min)	Heating Delay (min)	Heating Rate (degC/min)	Data file name
200	4.750	0.132	2.850	0.147	CP2101-21
500	3.750	0.226	2.550	0.265	CP2101-20
900	3.550	0.253		0.280	CP2101-19

Eng. Prototype 2 w/ short bag and non-insulated evaporator

Flow rate (mL/min)	Cooling Delay (min)	Cooling Rate (degC/min)	Heating Delay (min)	Heating Rate (degC/min)	Data file name
500	2.340	0.185	7.000	0.200	CP2101-11

FIGURE 11

Insulation appears to improve cooling rates but surprisingly worsens delay times. Longer bags appear to improve cooling rates somewhat. In all cases cooling rates become faster as flow rate increases as expected. Time delays and cooling rates of Engineering Prototype 1 are faster than Engineering Prototype 2. Cooling rate comparison is revisited again and data taken using Engineering Prototype 1 on animals are compared to data taken using Engineering Prototype 2 on the "Pig Simulator" as follows. With the valve open 100% and the heater off (no cooling or heating) and at 500 mL/min flow rate up till time 49.6 min the flow was turned off momentarily and the valve was set to 0% for maximum cooling (heater off) to allow the plate to reach 10°C. This happened quite fast at 50.1 min and the flow was set at 500 mL/min. This data plot is compared to the data plot shown in Figure 4. Comparison reveals smaller time delay and faster cooling rate, 0.2°C/min in Engineering Prototype 2 versus 0.17°C/min in Engineering Prototype 1. It also shows a small temperature difference between plate and inflow temperatures in Engineering Prototype 2, ~0.5°C compared to ~5°C in Engineering Prototype 1. This means that the longer bags result to more efficient heat transfer as expected.

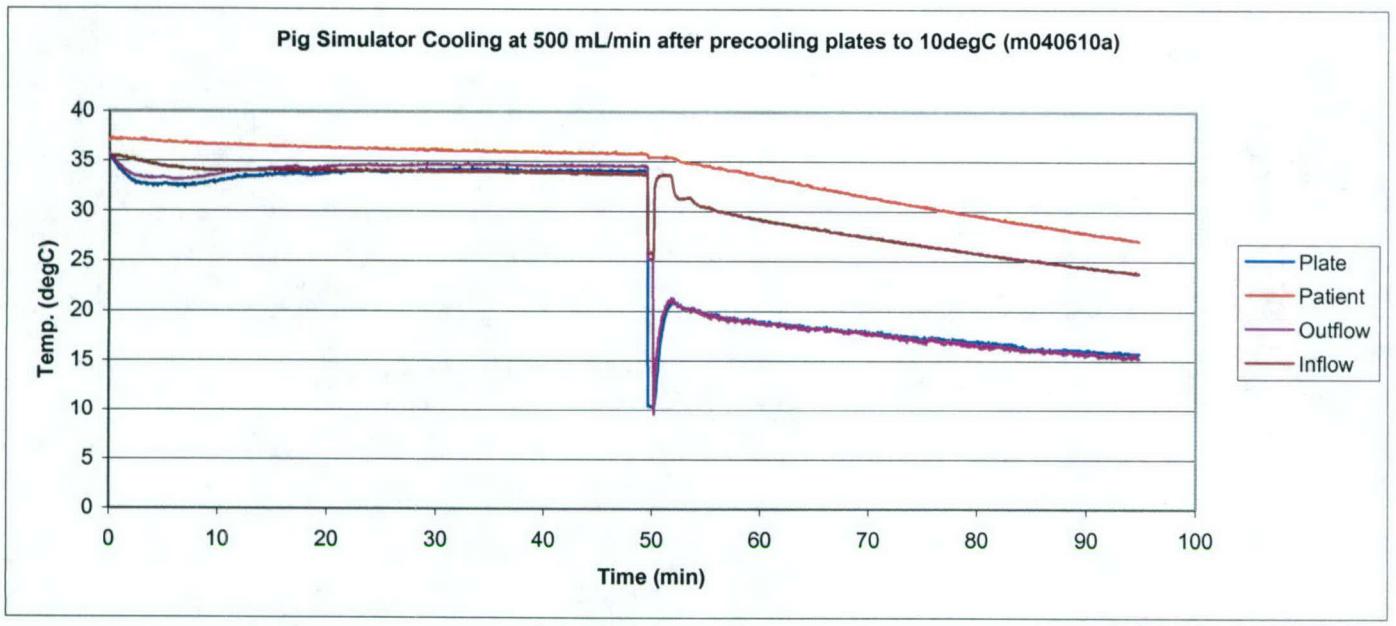


FIGURE 12

Conclusions

Engineering Prototype 1 exhibits a patient cooling rate that exceeds expectations but also exhibits clumsy patient temperature stabilization. Engineering Prototype 2 is a refined version albeit with slower patient cooling rate but improved stabilization within specifications. I recommend using the described configuration, which should be used in the design of the Clinical Prototype.

Suggestions for Further Work

Temperature measurements and characterization should be repeated in the Mild-Moderate Clinical Prototype and compared to Engineering Prototype 2.

Appendix C

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00015

TITLE OF TECHNICAL REPORT			REVISION
Evaluation of the accuracy of the OMEGA FLR-1600/FLV-4600 series water flow meter.			00
PROJECT OR PROGRAM NAME		PROGRAM NUMBER	DATE
Hypothermia		2004-03	06/08/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT			NAME OF AUTHOR
Flow Meter Accuracy			Christina Park
TECHNICAL AREA			
Measurement			
SUBJECT AND KEY TECHNICAL WORDS			
Hypothermia			
DOCUMENTATION TYPE			
☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☒ Other
ASSOCIATED REPORTS			

Abstract

The Omega water flow meter (FLR-1600 / FLV-4600 Series) was tested for the accuracy of its flow measurements. The readings from the flow meter were compared to calculated values, which were found by recording the time it took to fill a one-liter tube with water. The first experiment was run using regular tap water, and the second experiment was run using distilled water. Switching water types did not make a difference. The readings from the flow meter decreased as time passed, proving that the meter is working improperly even after it was returned to Omega once for repairs.

Background

In experimental, engineering and future production, the flow meter provides a means for testing the accuracy of the flow rate. When the flow meter was first purchased, it was tested and found to be off by 30%. Incidentally at that time Omega issued a recall notice regarding a problem with the embedded software in tarring the reading. The meter was returned to Omega, received back, and tested again. The 30% error was still present. The unit was sent to Omega again for calibration, received back, and tested once again as described here in.

Introduction

I tested the accuracy of the flow meter, which had been returned to Omega previously because it was not working properly. The meter was returned back to us and tested again for accuracy. I compared the readings given by the flow meter to the calculated values I had recorded by testing the amount of time it took to fill a one-liter tube with water.

Purpose

In writing this report, I intend to show the inaccuracy of our Omega FLR-1600 water flow meter.

Description of Apparatus and Setup

The test was setup as in figure 1.

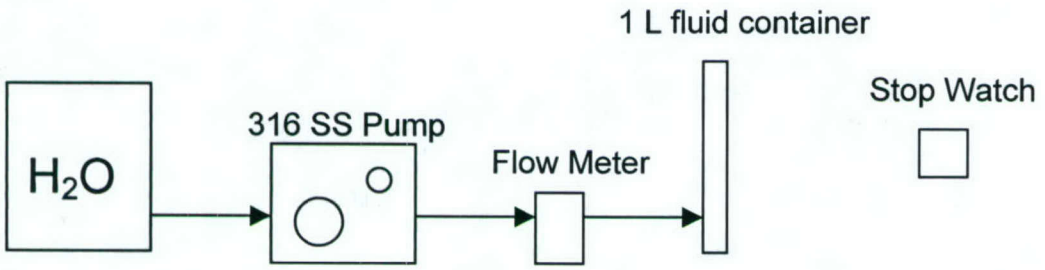


Figure 1. Test setup.

The Omega water flow meter (P/N: FLR-1605A-NIST, Serial #: 18084) was connected to a Cole Parmer 316 SS Magnetic Drive Pump (P/N: U-75225-10, Serial #: 1034344, Model # O/C c.8A), using LS25 Master Flex tubing. One end of the LS25 tubing went from the 316 SS pump to the water source, and the other end was connected to the flow meter using the LS25 Master Flex tubing. From the flow meter another piece of LS25 tubing was inserted into the one-liter plastic tube used for catching the water. An arbitrary flow rate was set on the pump and simultaneously the pump and stopwatch were started. The flow rate reading on the Omega meter was recorded periodically through out the testing procedure. Once the one-liter of water was obtained, the stopwatch and pump were stopped and the time was recorded.

The test was repeated three times. The first test was run using ordinary tap water, the second test was run using distilled water, and the third test was run using deionized water, which was recommended by the manufacturer.

Summary of Data and Results

The table in Figure 2 summarizes the measured and calculated results of the flow rates using the ordinary tap water, and varying the flow rate. The meter is clearly not working correctly which can be seen by the decreasing flow rate readings at a set flow rate from the pump.

Speed	Time/ 1 Liter (sec)	Meter readings	Cal. Flow Rate (L/min)
1	381	0.32, 0.32, 0.31, 0.29, 0.27, 0.25, 0.24, 0.20	0.157
2	156	0.65, 0.62,0.60, 0.59	0.385
3	85	1.31, 1.21, 1.17, 1.34	1.132
4	53	1.93, 2.02, 2.00	1.132
5	38	2.02	1.579
6	29	2.02	2.069

Figure 2: Data results using tap water.

The table in Figure 3 summarizes the measured and calculated results of the flow rates using distilled water and varying the flow rate. Again, it is clear to see that the meter is not working correctly due to the decrease in flow rate readings at a set flow from the pump.

Speed	Time/ 1 Liter (sec)	Meter readings	Cal. Flow Rate (L/min)
1	363	0.46, 0.44, 0.43, 0.41, 0.40, 0.38, 0.37	0.165
2	165	1.08, 1.10, 1.09, 1.07, 1.06, 1.04, 1.03, 1.02	0.364
3	109	1.36, 1.39, 1.37, 1.36, 1.34, 1.33, 1.28	0.55

Figure 3: Data results using distilled water.

The test was run a third time using deionized water with similar results to the first two tests.

Conclusions

The flow meter was found to be inaccurate and would be impossible to use for verifying the flow rate of other equipment.

Suggestions for Further Work

Omega will need to be contacted to either have this flow meter exchanged with a new one, or we will need to purchase a different flow meter which can be used with regular tap water.

Appendix D

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00023

TITLE OF TECHNICAL REPORT		REVISION
Flow Rate Accuracy in Mild-Mod BTP and Profound EP 2		00
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-02, 2004-03	7/09/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Verification	Christina Park	

TECHNICAL AREA

SUBJECT AND KEY TECHNICAL WORDS

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☒ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

Abstract

The accuracy of the flow rate in the Mild-to-Moderate and Profound BenchProto units was tested with the Omega #FLR1G06-loaner flow meter (Model# FLR-1605, Serial #16769). The flow meter was inserted into the tubing circuit after the pump and the flow readings were then recorded. The test was run initially with ambient temperature fluid, and repeated on both units when the fluid was chilled. The test was run a third time on the Mild-to-Moderate when the fluid was heated. With these tests we were able to verify whether the fluid temperature had any effect on the flow accuracy. The Omega meter proved the flow rates of the devices to be fairly accurate and the temperature change in fluid did not seem to affect the flow accuracy significantly.

Background

The accuracy of the flow rate in both the mild-to-moderate and profound hypothermia devices is critical to their functionality. Depending on the procedure being performed, a physician, EMT, etc., needs to be able to specify a flow rate and be confident that they're getting the resultant flow from the device no matter what the temperature of the fluid.

Introduction

With the mild-to-moderate and profound prototype devices being finished, the flow rate accuracy of the machines needed to be tested. Both devices use a Masterflex L/S, Easy-Load pump. The test was performed setting the pump at various flow rates and the results were recorded.

Purpose

Precise flow control is essential in the performance of the profound and mild-to-moderate hypothermia devices. In order to verify the accuracy of the flow control, the Omega flow meter was used to record the flow.

Description of Apparatus and Setup

The mild-to-moderate and profound devices were designed to have variable flow rates. The flow rate accuracy is to be within ±10% of the set point flow rate. The BenchProto set up is such that both units may be simulated simply by changing the software program used. Initially the BenchProto was setup to simulate the Mild-to-Moderate hypothermia device. The program was loaded, and the HyperTerminal program was setup to record the temperature data. The Pig Simulator was then connected to the disposable set of the BenchProto, inserting the Omega FLR1G05 flow meter into the tubing circuit before the disposable blood bag. YSI #44004 temperature sensors were used for fluid temperature readings (2252 @25°C, thermistor Mix "B"), which were saved in the HyperTerminal program. The sensors have an accuracy of ±0.2°C from 0°C to 60°C, and ±0.1°C from 32°C to 42°C (Yellow Springs Instruments data sheet). A Masterflex L/S, Easy-Load pump head (Model #77201-60) was used to produce the fluid flow. The device flow rates were set at 200, 500 and 900 mL/min. The procedure was run three times, the first running the fluid at ambient temperature, the second running a chilled fluid, and the third running warmed fluid through the disposable set. Once the procedure was finished, the data was then saved in a text file containing time stamps of when taken. The data then was processed by the extract.tcl program to be formatted in columns for importation into a spreadsheet (EXCEL).

The device was then setup to simulate the Profound Hypothermia device. A 10L fluid bag was connected to the Masterflex L/S, Easy-Load pump head to produce the fluid flow. The fluid was then pumped through the Omega FLR1G05 flow meter and discarded into a holding reservoir. The Profound tests were run using flow rates of 500, 1,000, 1,500, and 2,000 mL/min. This procedure was performed twice, the first time with ambient fluid and the second with chilled fluid.

Summary of Data and Results

To determine the flow rate accuracy of the Mild-to-Moderate and Profound devices, an Omega FLR1G05-loaner flow meter was connected to the tubing circuit. A temperature sensor was placed into the inflow to record the temperature being pumped into the patient.

The first test setup used the BenchProto to simulate the Mild-to-Moderate hypothermia device. The Pig Simulator was connected to the BenchProto, and water at ambient temperature was circulated through the disposable set at various flow rates. The results can be seen in Table 1 and Figure 1. At the 200 mL/min flow setting, an average flow of 196.3 mL/min was obtained. This gave an error of only 1.85%. At 500 mL/min flow setting, an average flow of 496.1 mL/min was obtained. This flow reading produced an error of 0.78%. At the final flow rate of 900 mL/min, an average flow of 917.3 mL/min was obtained, producing an error of 1.9%.

The second test used the same test setup, but pumped chilled fluid through the system rather than ambient. The results can be seen in Table 2 and Figures 2 a-c. In figure 2c, as the temperature of the fluid drops, the flow accuracy tends to drift. The Mild-to-Moderate device is required to stay above 6°C so any flow measurements below this temperature point would be out of the scope of the device. At 200 mL/min flow rate setting, an average flow was found to be 171 mL/min, producing an error of 14.5%. At a flow rate setting of 500 mL/min, an average flow was found to be 514.33, with an error of 2.86%. However, at 900 mL/min, the temperature accuracy declines dramatically. An average flow reading was found to be 1195.17 mL/min with an error of 32.8%.

A third test was then run using the same test setup, but pumped warmed fluid through the system with a constant flow rate of 500 mL/min. The results can be seen in Figure 3. An average flow for the warmed fluid was found to be 341.6 mL/min, which produced an error of 31.7%.

The fourth test setup was simulating the Profound Hypothermia device using the BenchProto. Various flow rates were initiated using ambient temperature water. The results can be seen in Table 3 and Figure 4. At a set point flow rate of 500 mL/min, an average flow was found to be 405.4 mL/min, with an error of 18.92%. With a flow rate set point of 1,000 mL/min, an average flow was found to be 874.8, with an error of 12.52%. In the third setup with a set point flow of 1,500 mL/min, an average flow as found to be 1356.6 mL/min, with an error of 9.56%. The last test setup had a flow rate set point of 2,000 mL/min, and had an average flow rate of 2,049.4 mL/min and an error of 2.47%.

The final test setup again simulated the Profound Hypothermia device using chilled water to run through the system. The results can be seen in Figure 5. At a flow rate set point of 50 mL/min, an average flow was obtained at 50.3, with an error of 0.6%. With a 100 mL/min set point, an average flow was found to be 80 mL/min, with an error of 20%. At the set point flow rate of 200 mL/min, an average flow was found to be 256 mL/min, with an error of 28%.

Mild-to-Moderate Device at Ambient Temperature

200 mL/min (Series 1)	500 mL/min (Series 2)	900 mL/min (Series 3)
198	497	988
219	432	966
199	475	902
205	502	911
202	514	910
182	491	907
185	517	875
190	508	902
191	530	895
192	495	917

Table 1

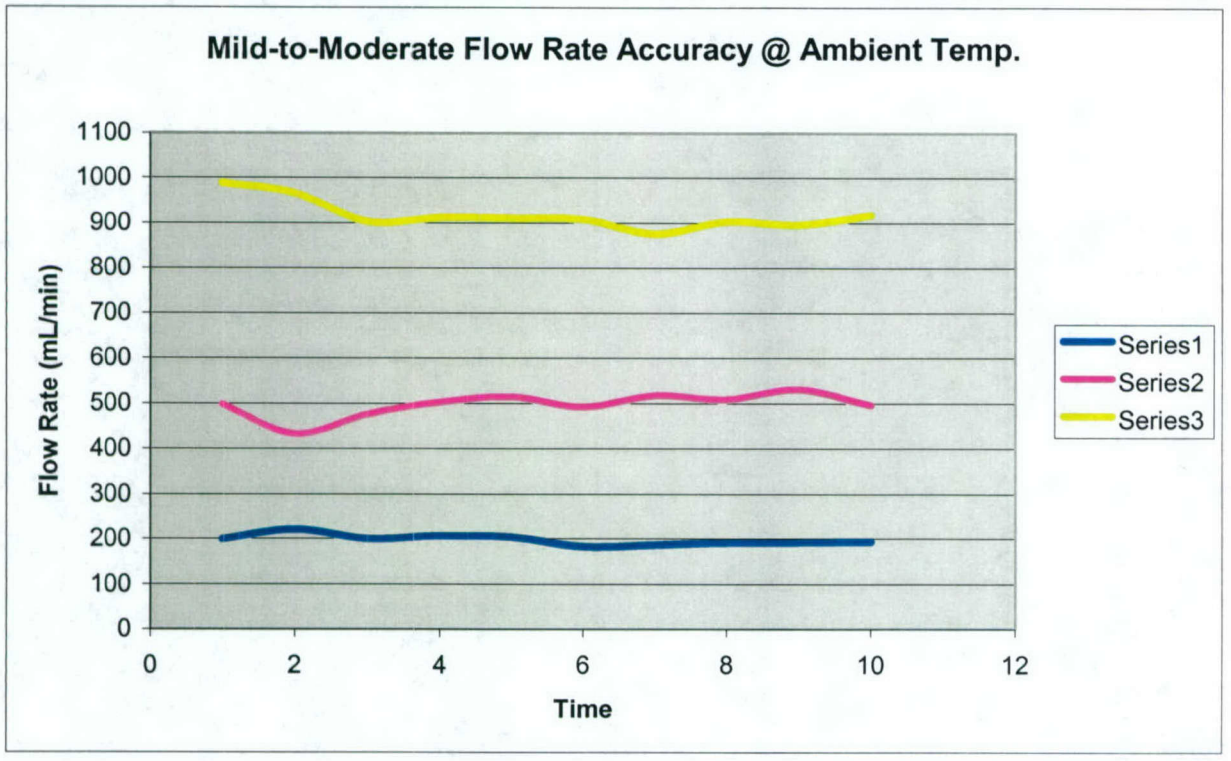


Figure 1

	200 mL/min	500 mL/min	900 mL/min
Average Flow:	196.3	496.1	917.3

Mild-to-Moderate Device Using Chilled Fluid

200 mL/min	Outflow Temp (degC)	500 mL/min	Outflow Temp (degC)	900 mL/min	Outflow Temp (degC)
207	18	514	12.6	1,082	10
167	16	531	12	1,206	9.5
185	15	517	11.5	1,190	9
191	14	506	11	1,215	8.8
140	13	503	10.5	1,220	8.5
136	12	515	10	1,258	8.2

Table 2

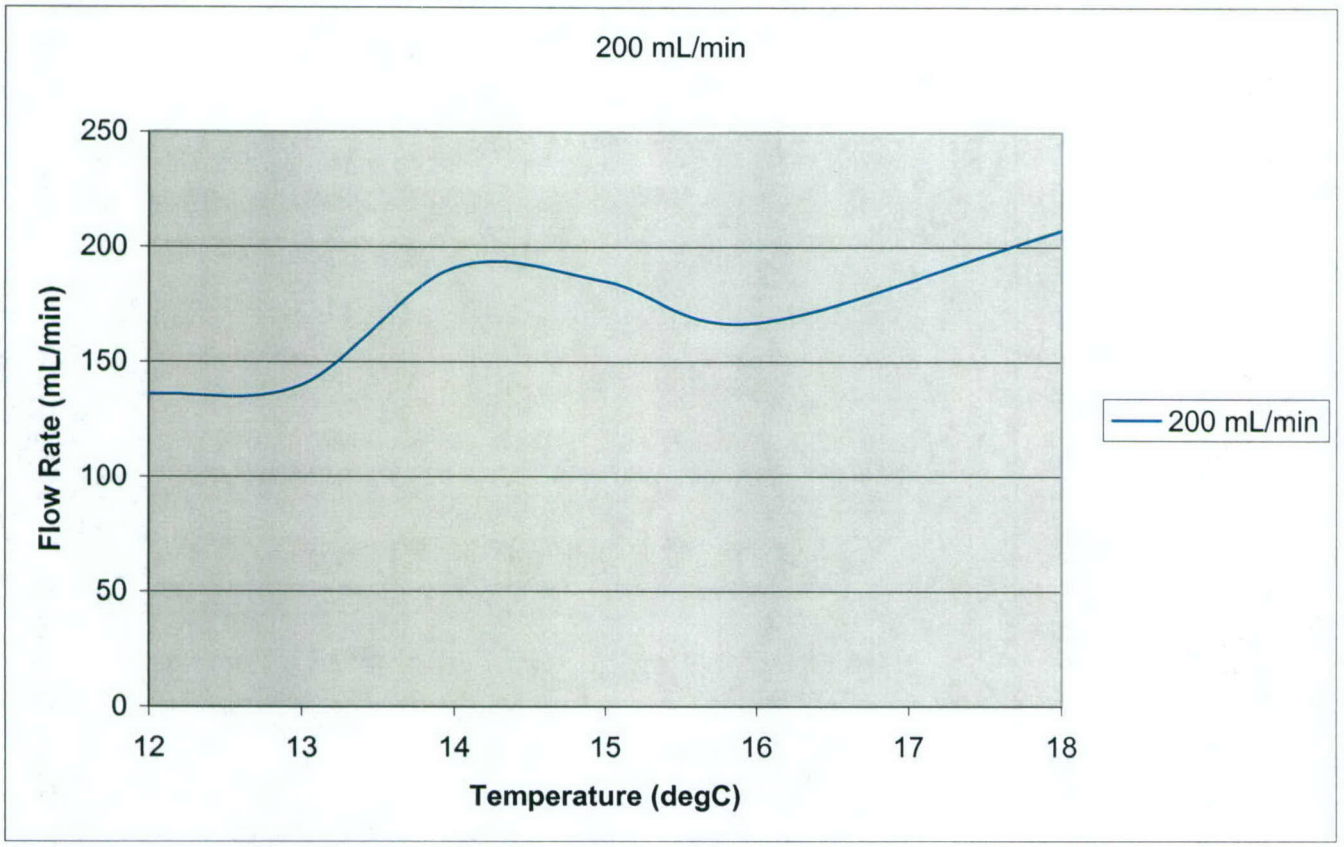


Figure 2a

	200 mL/min	500 mL/min	900 mL/min
Average Flow:	171	514.33	1195.17

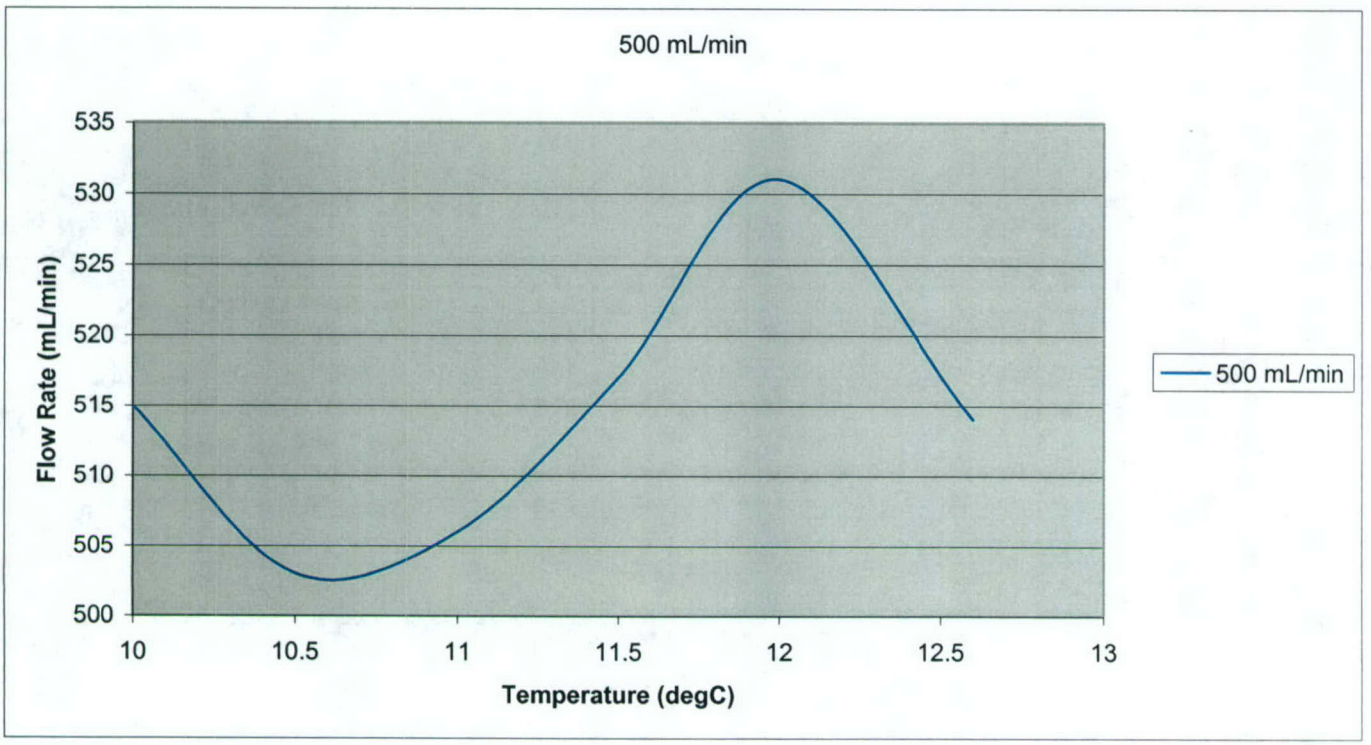


Figure 2b

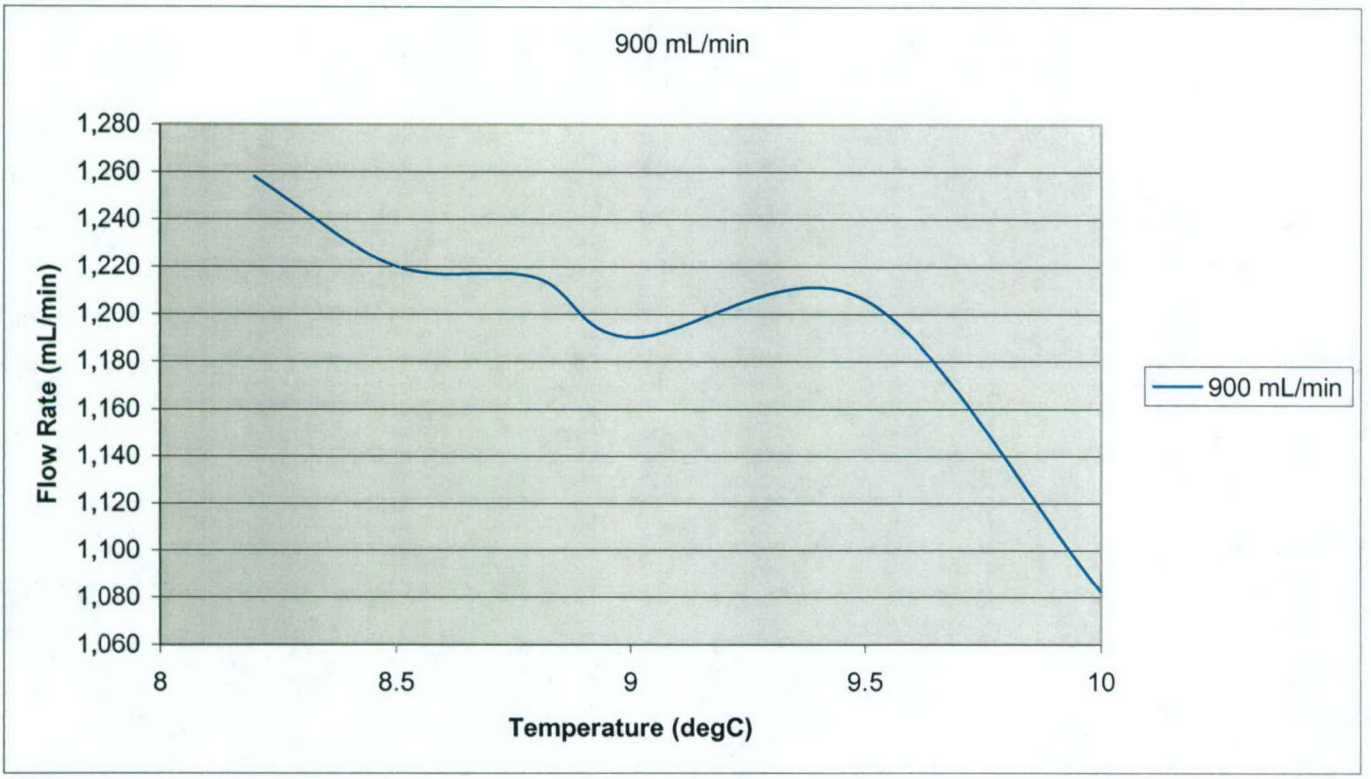


Figure 2c

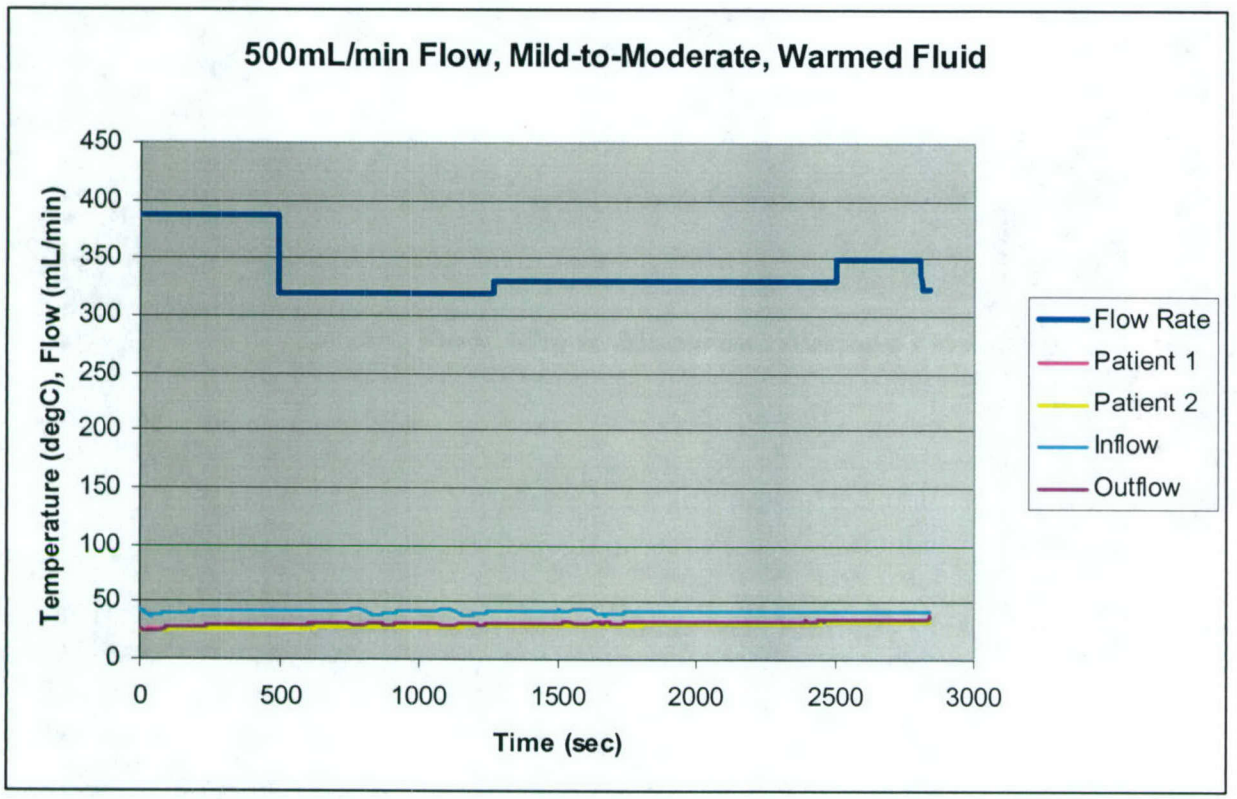


Figure 3

Profound at Ambient Temperature

500 mL/min	1,000 mL/min	1,500 mL/min	2,000 mL/min
410	775	1340	2014
408	856	1380	2022
397	919	1373	2011
408	925	1330	2108
404	899	1360	2092

Table 3

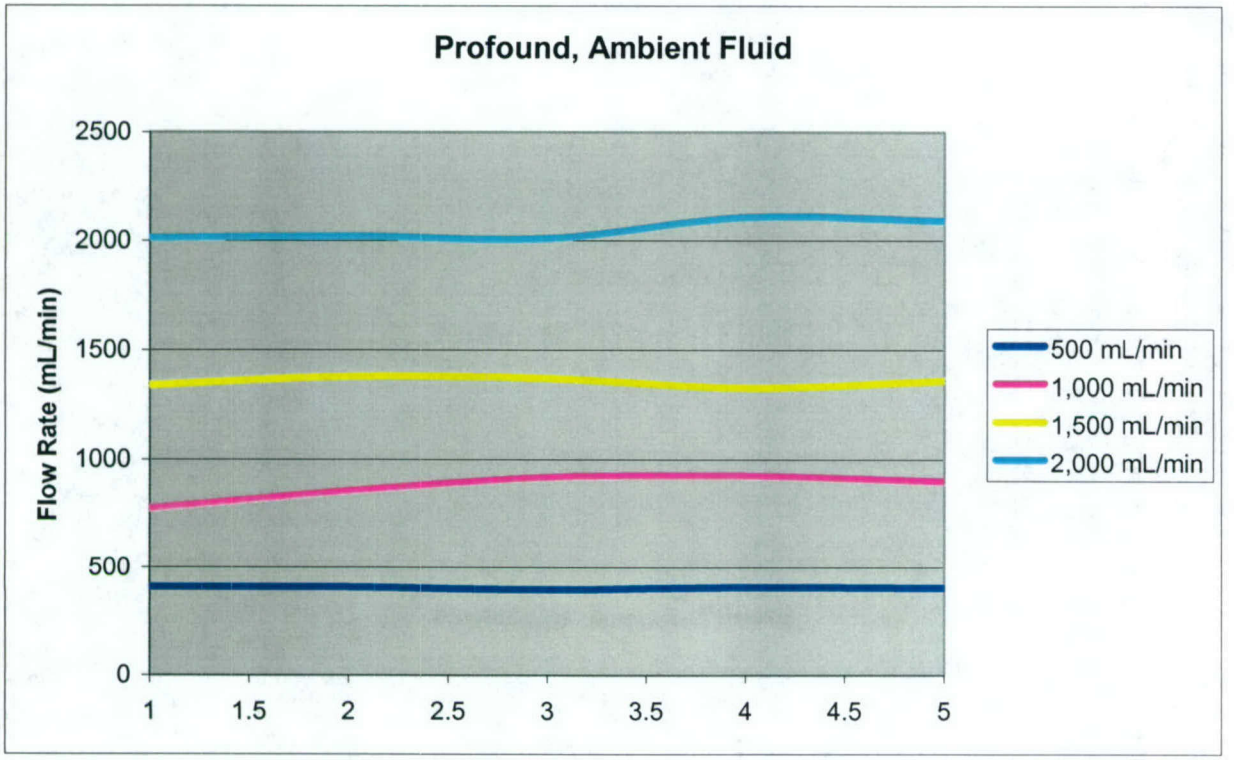


Figure 4

	500 mL/min	1,000 mL/min	1,500 mL/min	2,000 mL/min
Average Flow:	405.4	874.8	1356.6	2049.4

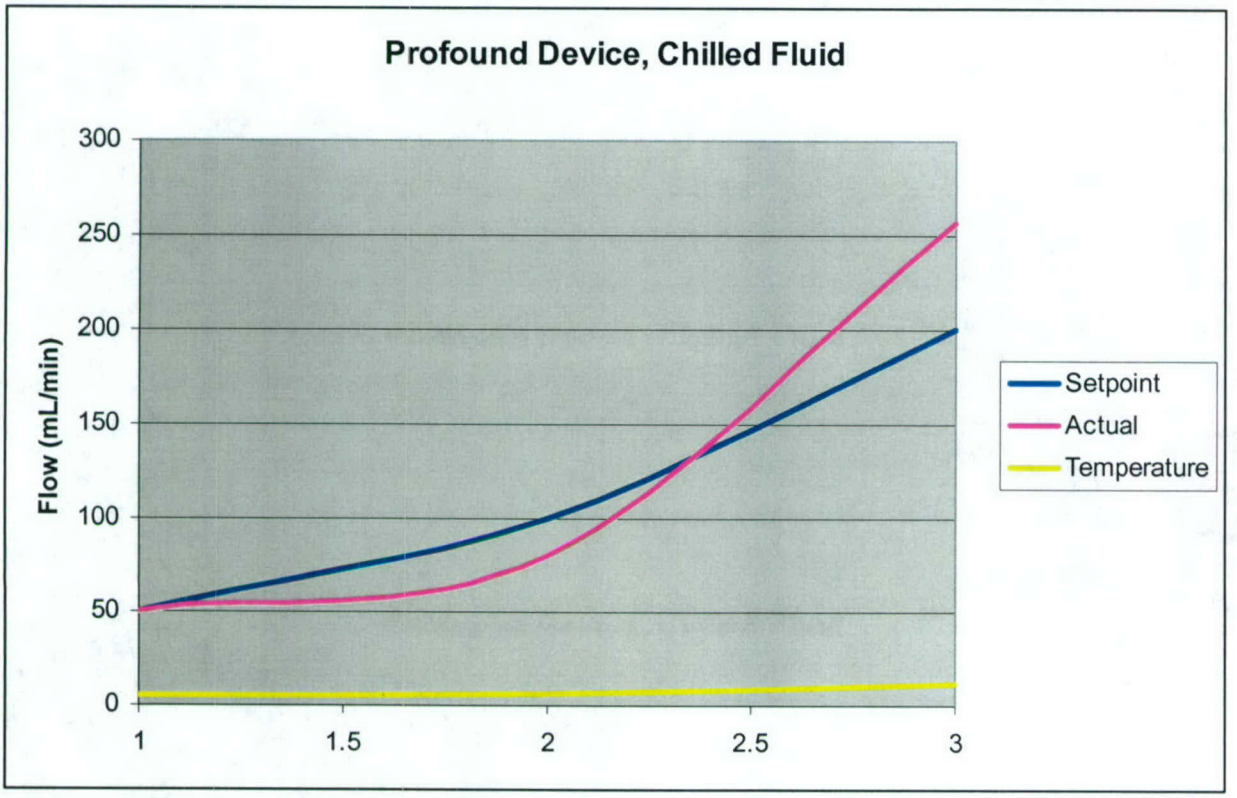


Figure 5

Conclusions

The accuracy of the flow settings was found to be poor when using a fluid any temperature other than ambient. The first test using the Mild-to-Moderate device and ambient temperature fluid performed the best having all flow setpoints perform within the tolerance. Using the Mild-to-Moderate setup and the chilled fluid produced inaccuracies with only the 500 mL/min flow setting falling within tolerance. The Mild-to-Moderate device using warmed fluid performed the worst, not having one set point fall within the tolerable range.

The Profound hypothermia accuracy was even less stable than the Mild-to-Moderate. When running the first test with the ambient fluid, only 1,500 and 2,000 mL/min flow rates were within the tolerable range. When running the device with the chilled fluid the device fell within tolerance only with a 50 mL/min fluid flow rate.

Suggestions for Further Work

More work needs to be done on both the Mild-to-Moderate, and Profound devices so that the accuracy of the flow rates can be improved upon. Both devices need to be able to perform accurately with cooled and warmed fluid due to the fact that during a medical procedures ambient temperature fluid will not be used. Other means of controlling this flow rate need to be explored.

Appendix E

ARDIEM

TECHNICAL REPORT

RECORD NO.
AM-00012

TITLE OF TECHNICAL REPORT			REVISION
Bubble Detection Definitions and Evaluation			0
PROJECT OR PROGRAM NAME		PROGRAM NUMBER	DATE
Hypothermia		2004-02	04/21/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT			NAME OF AUTHOR
Bubble Detection Testing			Mike Pitsakis
TECHNICAL AREA			
Test, Measurement			
SUBJECT AND KEY TECHNICAL WORDS			
Hypothermia			
DOCUMENTATION TYPE			
☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☒ Other
ASSOCIATED REPORTS			

Abstract

The introduction of even a small amount air in arteries/veins causes an embolism with dangerous physiological effects. There is uncertainty regarding air bubbles less than 40 mm diameter that will cause damage. Commercially available blood filter/bubble traps can limit air bubbles to 40 μm diameter while commercially available bubble detectors respond to 20 μL volume or larger. Two Introtek bubble detectors were evaluated experimentally (one for Masterflex LS18 and one for LS25 tubing sizes) and both were found to respond to 20 μL or larger bubbles.

Background

In an Ardiem Medical meeting with SCRR staff on February 10, 2004 in Pittsburgh, the SCRR staff requested that a bubble detector be employed, together with a tubing occluder, in addition to the filter/bubble trap in the extracorporeal circuit of both Mild-Moderate and Profound Hypothermia Induction devices. In finding a reference to a quantified bubble size, that when detected, triggers the occluding mechanism and shuts down the pump, we consulted Dr. Lyn Yaffe. The following is his expert response in an email dated Monday, March 22, 2004 5:54 PM.

"As of 2002, based on the review article below, there was still uncertainty about the impact of small bubbles (generally, I think, meaning below 40 microns) on cerebral injury. I cannot find more recent information. Certainly, bubbles 40 micron or larger can cause damage. The lower limit is difficult to set based on the literature. Maybe it should be around 20 microns or larger for pump off. For an aggregate of bubbles, I do not really know. If the aggregate is 40 microns or larger, for instance, but the individual bubbles are each less than 10 microns, is it still a problem? I do not know for sure. Maybe an aggregate should simply be treated as a large bubble and the pump should be cut off? Bubbles in an aggregate could coalesce to actually form a single larger bubble I suppose, so maybe the strategy should be to view an aggregate as a large bubble.

The pathophysiology of cerebral arterial gas embolism. Mitchell S, Gorman D.; The Wesley Centre for Hyperbaric Medicine, Brisbane, Australia. smitchell@wesley.com.au; J Extra Corpor Technol. 2002 Mar;34(1):18-23.

Bubbles are introduced to the arterial circulation in many patients undergoing cardiac surgical procedures, and some of these distribute to the cerebral vessels. Larger bubbles may arrest in cerebral arterioles, causing ischemia and neuronal injury in the downstream territory. Smaller bubbles may redistribute through the cerebral circulation, but this is not a benign event. Their passage may cause transient ischemia and cause damage to endothelium. Margination and activation of leukoctyes follows, and may cause a secondary ischemia. Although the potential of large bubbles to cause cerebral injury is not disputed, there is controversy over the significance of exposure to small bubbles in cardiac surgery. It is known that postsurgical neuropsychological deficits do correlate positively with numbers of emboli to which patients are exposed, but to date, the technology to distinguish between gaseous and particulate emboli or to size emboli accurately is not readily available. Until this technology becomes available and is applied in large studies designed to determine the importance of small bubbles, it seems prudent to take all practical steps to prevent introduction of arterial bubbles in cardiac surgery. Publication Types: Review; Review, Tutorial; PMID: 11911624 [PubMed - indexed for MEDLINE]

In the article's abstract below, from Jan 2004, there is concern for both bubbles >40 microns (large bubbles, I think) and <40 microns (small bubbles, I think). The article says that elimination of bubbles >40 microns was better achieved with a dynamic bubble trap (DBT) versus an arterial filter, and that reduction of bubbles <40 microns was the same for a DBT and the arterial filter. Authors noted that combined techniques were 94% effective in eliminating bubbles.

Elimination of microbubbles from the extracorporeal circuit (ECC): dynamic bubble trap versus arterial filter. Martens S, Dietrich M, Pietrzyk R, Graubitz K, Keller H, Moritz A., Department for Thoracic and Cardiovascular Surgery, University Hospital J.W. Goethe, Frankfurt am Main, Germany; martens.herz@gmx.de; Int J Artif Organs. 2004 Jan, 27(1):55-9.

BACKGROUND: Open heart surgery is associated with important risk of cerebral and peripheral organ dysfunction, attributed in part to microbubbles generated in or not eliminated from the ECC. For elimination of microbubbles, a dynamic bubble trap (DBT) was developed for the arterial line of ECCs. METHODS: Bubble eliminating properties of an arterial filter were evaluated in four CABG patients and compared to the performance of the DBT in four patients. One patient received both devices. RESULTS: Elimination of bubbles between 40-120 micron was significantly higher with the DBT (88% vs. 57% with arterial filter, p=0.034). Reduction of bubbles below 40 micron was equivalent in both groups. The combination of both devices was most effective (94% for bubbles >40 micron). CONCLUSION: Arterial filter and DBT are equally effective in elimination of smaller gas bubbles. However, bigger bubbles possibly causing cerebral and peripheral organ damage are eliminated to a greater degree by the DBT. PMID: 14984184 [PubMed - in process]

The next paper showed that a dynamic bubble trap reduced cerebral embolism during CPB by measuring the S100 Beta serum indicator of possible neurologic injury, indicating that an arterial filter alone may not be sufficient, in agreement with the previous paper.

The dynamic air bubble trap reduces cerebral microembolism during cardiopulmonary bypass. Schoenburg M, Kraus B, Muehling A, Taborski U, Hofmann H, Erhardt G, Hein S, Roth M, Vogt PR, Karliczek GF, Kloevekorn WP., Department of Thoracic

and Cardiovascular Surgery, Kerckhoff-Klinik, Bad Nauheim, Germany. markus.schoenburg@kerckhoff.med.uni-giessen.de; J Thorac Cardiovasc Surg. 2003 Nov, 126(5):1455-60.

OBJECTIVE: Neuropsychologic disorders are common after coronary artery bypass operations. Air microbubbles are identified as a contributing factor. A dynamic bubble trap might reduce the number of gaseous microemboli. METHODS: A total of 50 patients undergoing coronary artery bypass operation were recruited for this study. In 26 patients a dynamic bubble trap was placed between the arterial filter and the aortic cannula (group 1), and in 24 patients a placebo dynamic bubble trap was used (group 2). The number of high-intensity transient signals within the proximal middle cerebral artery was continuously measured on both sides during bypass, which was separated into 4 periods: phase 1, start of bypass until aortic clamping; phase 2, aortic clamping until rewarming; phase 3, rewarming until clamp removal; and phase 4, clamp removal until end of bypass. S100 beta values were measured before, immediately after, and 6 and 48 hours after the operation and before hospital discharge. RESULTS: The bubble elimination rate during bypass was 77% in group 1 and 28% in group 2 (P <.0001). The number of high-intensity signals was lower in group 1 during phase 1 (5.8 +/- 7.3 vs 16 +/- 15.4, P <.05 vs group 2) and phase 2 (6.9 +/- 7.3 vs 24.2 +/- 27.3, P <.05 vs group 2) but not during phases 3 and 4. Serum S100 beta values were equally increased in both groups immediately after the operation. Group 2 patients had higher S100 beta values 6 hours after the operation and significantly higher S100 beta values 48 hours after the operation (0.06 +/- 0.14 vs 0.18 +/- 0.24, P =.0133 vs group 2). Age and S100 beta values were correlated in group 2 but not in group 1. CONCLUSION: Gaseous microemboli can be removed with a dynamic bubble trap. Subclinical cerebral injury detectable by increases of S100 beta disappears earlier after surgical intervention. Publication Types: Clinical Trial; Randomized Controlled Trial. PMID: 14666019 [PubMed - indexed for MEDLINE]

The next article looks at bubbles as small as 10 microns to demonstrate the effectiveness of the Jostra Quart arterial filter.

Ex vivo testing of the Quart arterial line filter. Mueller XM, Tevaearai HT, Jegger D, Augstburger M, Burki M, von Segesser LK.; Clinic for Cardiovascular Surgery, Centre Hospitalier Universitaire, Lausanne, Switzerland; Xavier.Mueller@chuv.hospvd.ch; Perfusion. 1999 Nov;14(6):481-7.

Arterial line filters are now routinely used in cardiac surgery in order to decrease the microemboli load to the patient. The Quart filter (Jostra, Hirrlingen, Germany, http://www.jostra.de/index.php?page=66) with a new planar construction design, an easy de-airing system and an integrated bypass, was tested for air filtration capacity and resistance to blood path in a standardized setting with surviving animals. Three calves (mean body weight: 71+/-3.4 kg) were connected to a standard cardiopulmonary bypass (CPB) circuit by jugular venous and carotid arterial cannulation with a mean flow rate of 3.5 l/min. The arterial line filter was challenged with upstream injections of boluses of air of 5, 10 and 15 ml, respectively. A Doppler ultrasound was positioned downstream on the arterial line to measure bubble count and size. The pressure drop through the filter was monitored at flow rates of between 1 and 6 l/min. At the end of the procedure the animals were weaned from the CPB and, thereafter, from the ventilator. After 7 days, the animals were sacrificed electively. This study shows that important quantities of air can be injected into the arterial line upstream of the filter with small volumes of small sized bubbles recorded downstream. With the 5 ml air bolus injection, mean values of 0.3+/-0.6 bubbles of 30 and 40 micron were detected, whereas with the 20 ml bolus, 32.6+/-8.7 bubbles of 10 micron, 3.7+/-1.1 bubbles of 30 micron, 3.3+/-0.6 bubbles of 40 micron and 0.7+/-1.1 bubbles of 50 micron were recorded. The blood path resistance at different blood flow rates was well within the acceptable range with a pressure drop of 20+/-0 and 26.6+/-5.7 mmHg at flow rates of 4 and 5 l/min, respectively. With its planar concept, the Quart filter offers good air filtering capacity both in terms of bubble count and size after injection of large boluses of air, without any increase of resistance to the blood path. Moreover, it offers a venting function and an integrated bypass system. PMID: 10585156 [PubMed - indexed for MEDLINE]

Ultrasonic sensors for bubble detectors (http://www.zevex.com/appliedtechnology/ultrasonic.cfm) may offer an ultrasonic detector with a broad range for size detection – "Zevex's specialty is creating customized bubble detectors that meet your design requirements. Our ultrasonic air bubble detectors are currently used for non-invasive monitoring of infusion lines on a variety of medical instruments in order to protect the patient from air emboli infusion. Some specific applications include volumetric infusion pumps (bedside, pole mounted and ambulatory models), hemodialysis machines, blood collection and component separation instruments, and cardio-pulmonary bypass systems."

Other interesting sites for bubble detectors, which you are already probably aware, include:
http://www.introtek.com/html/technology.html
http://www.introtek.com/90-220Introtek.pdf"

We also asked Bill Stezoski of SCRR about the size of the bubble or bubbles that would prompt unit shut-down by the bubble detector. The following is his response in email dated Wednesday, March 03, 2004 1:11 PM.

"I **do not know** what size the commercial CPB bubble detectors are designed for --will communicate with our local Medtronic. rep (Gary Cello) for those stats. However, a 100 microliter (0.1ml) bubble is easily detectable with the naked

eye, I would assume that commercial units could easily detect 40-50 ul bubbles with ease. Our current blood filter traps go down to 20 ul".

Introduction

I ordered the Introtek BDF-BM12-S06 for LS18 platinum cured silicon tubing (profound) and BDF-BM12-S04 for LS25 tubing (mild-mod) bubble detectors for evaluation as recommended by Dr. Yaffe and also used in the Viacirq Thermochem 1000 device. Also ordered a BD3-4300-007 pulsed excitation/detection electronics board to be used with either bubble detector. This board operates at 12 VDC and offers a digital output and an on board LED to indicate the presence (LO state or OFF) or absence or air (HI state or ON).

Introtek's Ultrasonic Air Bubble Detectors utilize the characteristics of high-frequency acoustic energy to monitor tubing or vessels for the presence of air, air bubbles, foam, or liquid. A sensor containing piezoelectric crystals is placed in direct contact with the desired point of detection. Introtek's air detection sensors and electronics provide pulses of ultrasonic energy, which are sent through tubing and normally received within a specified "window" of time. If air becomes present, the ultrasonic signal does not arrive within this "window" of time and a warning or dry signal is immediately transmitted.

Purpose

Determination of the smallest bubble size that will trigger the bubble detector/occluder mechanism is the purpose of this work.

Description of Apparatus and Setup

I set up a tubing circuit consisting of a 5-gallon container filled with tap water, a Master-Flex L/S pump (Digital Standard Drive and Easy Load II pump head), a blood filter/bubble trap (Terumo Cardiovascular Systems AV6SV), a bubble detector, and a flow meter (Omega FLR-1600 Water Flowmeter) for two separate experiments. I connected, to the electronics board output, a frequency counter (Escort EUC-2200 !75 MHz Universal Counter) that was set to operate in pulse counter mode. The counter would respond to any positive transition so that I didn't have to rely on observing the LED indicator. I started the pump and fluid circulation at 500 mL/min, let it stabilize, then injected air in the tubing, before the bubble detector, using a 1mL 27G BD U-100 insulin syringe with 2 unit subdivisions (20 mL). I repeated at 1 and 2 L/min for the LS18 tubing.

The only difference between the two experiments was the tubing size and the size of the bubble detector: Introtek BDF-BM12-S06 for LS18 tubing and Introtek BDF-BM12-S04 for LS25 tubing.

Also I developed a spreadsheet \\ARDIEMFS\RD\5-Engineering\Systems Eng\Hypothermia\Analysis\Conv_Bubble&Flow.xls for conveniently converting between bubble diameter and volume and vice versa.

Summary of Data and Results

In either experiment above, injecting one syringe subdivision of air or ~20 mL or more was detected by the respective bubble detector. It's worth mentioning that I did not notice the LED indicator flickering at any flow rate unless a very large volume of air was injected or the tube was removed from the bubble detector.

Conclusions

The following bubble detectors are capable of detecting air bubbles as small as 20 μL (2.77 – 3.73 mm diameter): Introtek BDF-BM12-S06 for LS18 tubing and Introtek BDF-BM12-S04 for LS25 tubing. Note that the blood filter/bubble trap is specified by the manufacturer to block air or particles larger than 40μm diameter this corresponds to an extremely small volume of 3.35E-11 L for a spherical bubble. It is imperative that the blood filter/bubble trap be placed before the bubble detector to avoid continuous triggering and activate the occluder only if the blood filter/bubble trap fails.

Suggestions for Further Work

The bubble detectors will be verified in the development phase as part of either device.

Appendix F

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00014

TITLE OF TECHNICAL REPORT		REVISION
Evaluation of Pressure Measuring Components and Measurement of Pressure Ranges In Hypothermia Devices		00
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia		5/17/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT		NAME OF AUTHOR
Pressure Measurement Capability		Mike Pitsakis

TECHNICAL AREA

Sensors, Measurement

SUBJECT AND KEY TECHNICAL WORDS

Pressure, Flow

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	X Other

ASSOCIATED REPORTS

Abstract

A pressure measuring set up using a Motorola MPX2200DP pressure sensor and a Gish ECPML36 pressure manometer Isolator were used together with a reference pressure meter in the extracorporeal circuit of the Profound and Mild-Moderate device with the intent to evaluate these components. Also the pressure ranges exerted by the fluid in the disposable sets of the Profound and Mild-Moderate devices were determined by measurement. The pressure sensor and pressure isolator combination works well with readings that are closely correlated to the reference readings. The pressure above 700 mL/min in the Mild-Moderate case exceeds 7 psi and presents a limit inherent to the tubing. Catheter length should be limited to 4 feet or less to avoid excessive pressure build up.

Background

Measurement of fluid pressure in the extracorporeal circuit of either Mild-Mod or Profound Hypothermia Induction device requires an accurate sensor and a disposable membrane part that isolates the fluid from the sensor while transferring pressure from the fluid side of the extracorporeal circuit to the air side of the sensor. Standard L/S 25 tubing (1/4" ID platinum cured silicon) is used with the Mild to Moderate device while an L/S 18 (3/8" ID platinum cured silicon) is used with the Profound device. For animal experiments the following cannula sizes are used according to an email from Bill Stezoski of SCRR dated april 21, 2004.

"The cannula(s) **routinely used** in our SA rapid flush procedures is a # 6-gauge thin-wall (0.010 in) stainless steel tube; Size: 16 French (approx >5.0 mm) , i.e. OD = 0.203" ; ID = .183" or the smaller # 7-G (14F) cannula i.e. OD =.180"; ID = 160" (Most 20 kg dogs are cannulated with the # 7-G)".

Introduction

We selected for evaluation:

1. a Motorola MPX2200DP pressure sensor.
2. a Gish ECPML36 pressure manometer Isolator, 3/16 in I.D.

The sensor responds to differential air pressures from 0 to 29 psi producing a 0 – 40 mV output with +/- 0.25% linearity over 0 – 85 °C.

Purpose

The intension of the work described in this report is the evaluation of the pressure measuring components (Experiment I) and measurement of the pressure ranges exerted by the fluid in the disposable sets of the Profound and Mild-Moderate devices Experiment II).

Description of Apparatus and Setup

Experiment I

One port of the pressure isolator was attached to the tubing via a "T" fitting while the other port was attached to one of the pressure sensor ports. The other port of the pressure sensor was open to the atmosphere. A Cole Parmer EW-68110-10 digital pressure meter (0 – 30 psig, +/-1% accuracy) was also attached to the tubing via a "T" fitting and used to obtain reference readings. The pressure sensor was biased with +10 VDC by a bench power supply (HP 6214A) while its output was read by a multimeter (Fluke 23III). The Bench Prototype was used to circulate the fluid at rates 0 – 900 mL/min with L/S 25 tubing for Mild-Moderate and 0 – 2000 mL/min with L/S 18 tubing for Profound with the "Pig" Simulator at 2000 mL/min. Flow rate was set and reference pressure and voltage readings were recorded. Pressure sensor voltage readings were converted to pressure using 725 psi/V conversion factor (29psi/40mV). Note that it is not necessary for the tubing of the fluid side of the pressure isolator to be filled with fluid. As a matter of fact better results are obtained if there is little or no fluid in it.

Experiment II

I used the same set up as above except that I inserted a 4-foot long 3/32" ID tubing in the extracorproreal circuit to simulate the cannula/catheter.

Summary of Data and Results

Experiment I

The table in Figure 1 summarizes the pressure and voltage data taken plus the calculated pressure values and the discrepancy. These values are plotted versus flow rate in the graph shown in Figure 2. I believe the discrepancy is largely due to the 1/10 mV resolution of the DMM. There was a 0.6 mV offset at the pressure sensor output (at zero pressure with respect to atmospheric). The offset has been subtracted in the values listed.

Flow (mL/min)	Press Ref (PSI)	Volt Meas Adj (mV)	Press Calc (PSI)	Press Discrepancy (%)
200	1.59	2.2	1.595	-0.31
500	2.30	3.2	2.320	-0.87
900	3.26	4.5	3.263	-0.08

FIGURE 1

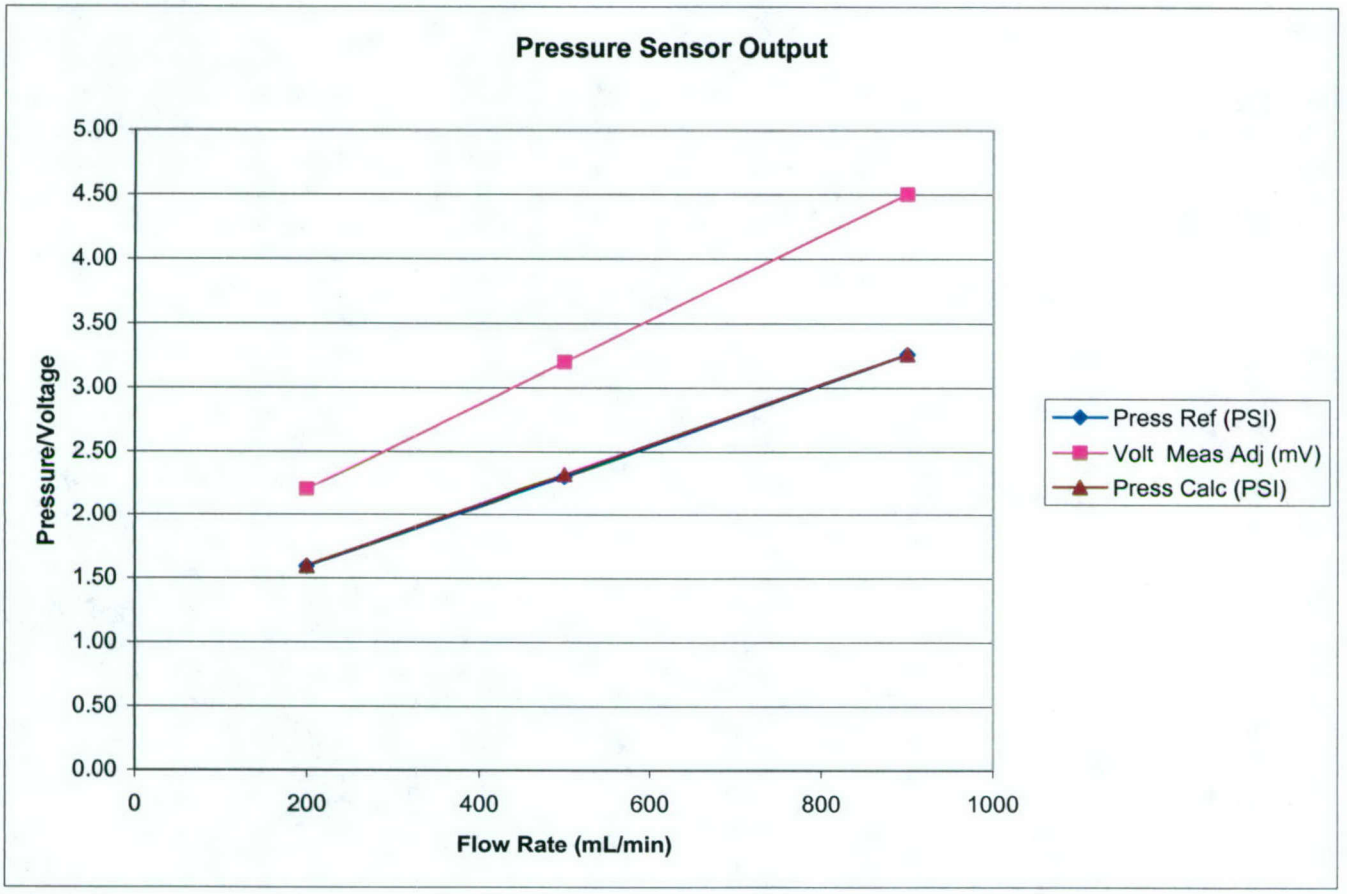


FIGURE 2

Experiment II

For the Mild-Moderate case, the table in Figure 3 summarizes the pressure taken at the listed flow rates plus the adjusted pressure values (subtracted the pressure at 0). These values are plotted versus flow rate in the graph shown in Figure 4.

Flow (mL/min)	Press Ref Adjusted (PSI)	Press Reference (PSI)
0	0	5.4
200	1.1	6.5
300	2	7.4
400	3	8.4
500	4	9.4
600	5	10.4
700	6.1	11.5
800	7.9	13.3
900	9.7	15.1

FIGURE 3

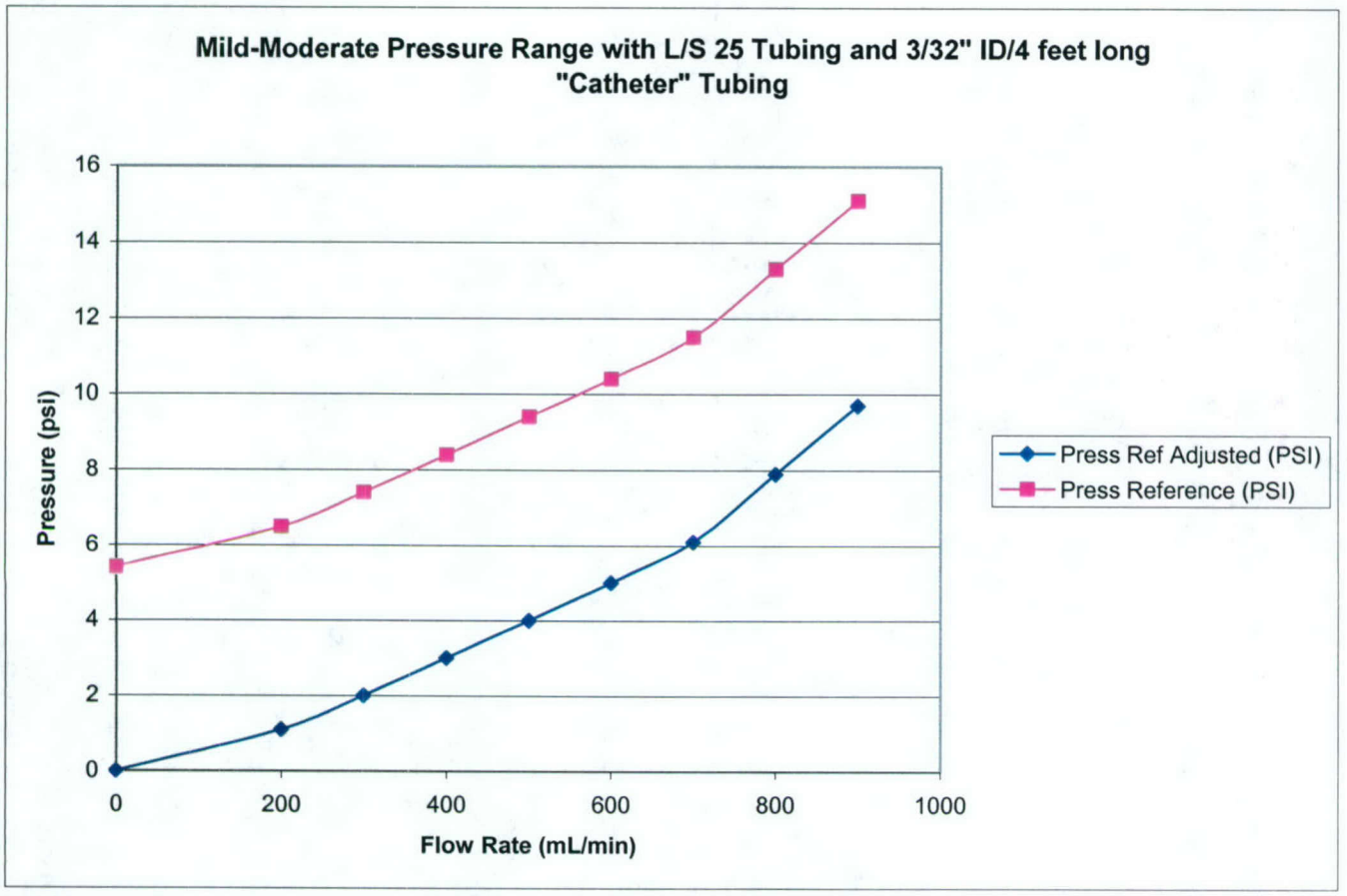


FIGURE 4

For the Profound case, the table in Figure 5 summarizes the pressure taken at the listed flow rates plus the adjusted pressure values (subtracted the pressure at 0). These values are plotted versus flow rate in the graph shown in Figure 6.

Flow (mL/min)	Press Ref Adjusted (PSI)	Press Reference (PSI)
0	0	5.4
300	2	7.4
500	2.3	7.7
1000	2.8	8.2

FIGURE 5

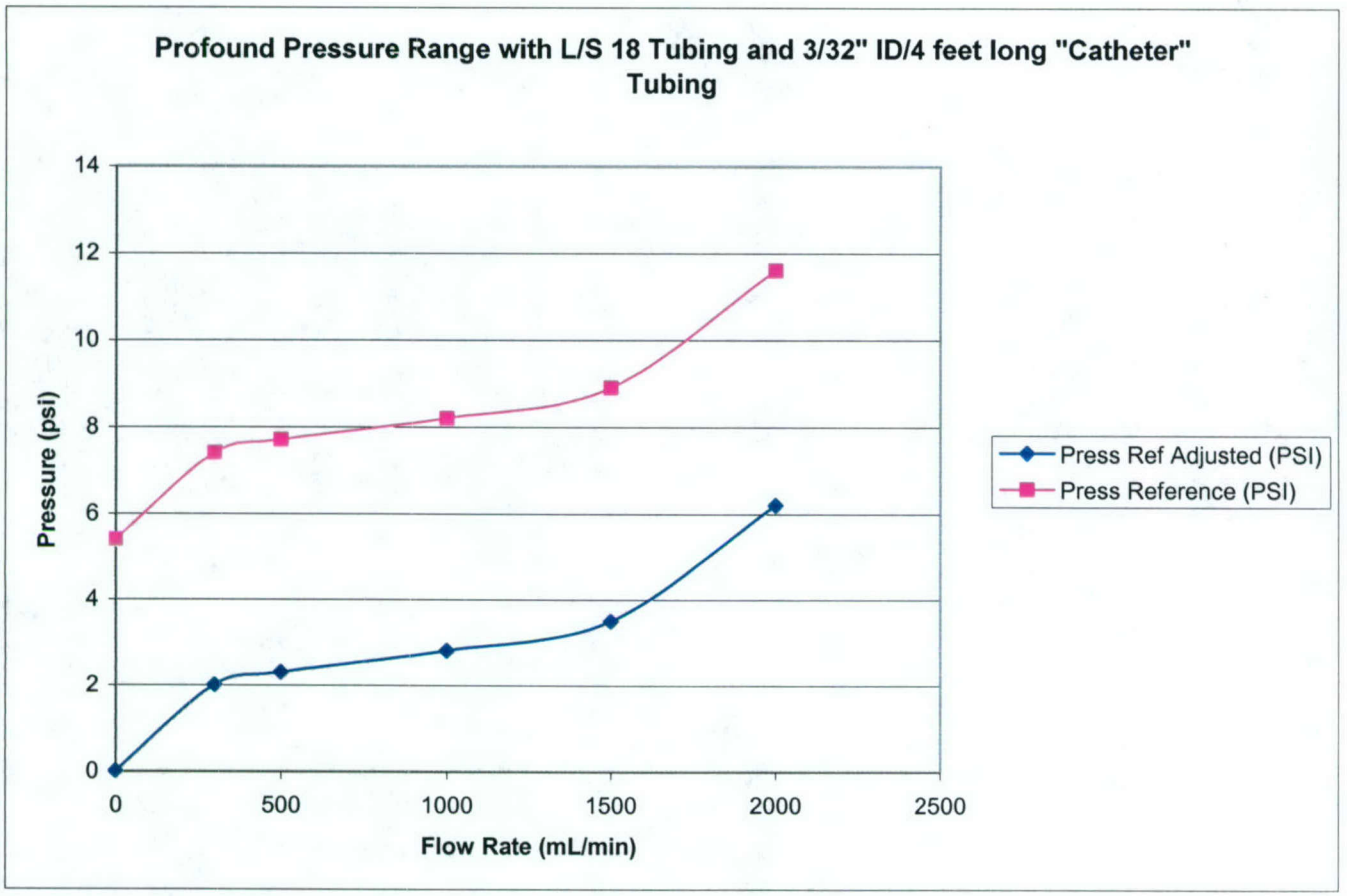


FIGURE 6

A longer piece of 3/32" ID tubing was also used to simulate a longer catheter. The pressure build up to 20 psi or more with the result of leakage from the myocardial temperature probe fittings (inflow and outflow), since the platinum cured silicon tubing is rated for 7 psi maximum the experiment was terminated.

The pressure without the catheter in either device disposable set stays below 4 psi at maximum flow rate.

Data conversions, tables, and plots were produced by the \\ARDIEMFS\RD\5-Engineering\Systems Eng\Hypothermia\AnalysisCalib_Pressure.xls spreadsheet.

Conclusions

The selected pressure sensor and pressure isolator combination works nicely producing pressure readings that are closely correlated to the reference readings (under 1% difference) and should be used in the devices.

The pressure versus flow relationship is nonlinear. The pressure above 700 mL/min in the Mild-Moderate case exceeds 7 psi and above it builds up rapidly and presents a limit inherent to the tubing. The pressure above 1500 mL/min in the Profound case builds up rapidly too but stays within 7 psi. The catheter simulating 3/32" ID tubing, however, is actually smaller than the cannula size making pressure higher than in reality. Catheter length should be limited to 4 feet or less to avoid excessive pressure build up.

Suggestions for Further Work

The experiments should be repeated and the results be confirmed on Engineering prototypes possibly using an actual catheter.

Appendix G

ARDIEM

DESIGN REQUIREMENTS DOCUMENT

Mild-to-Moderate Hypothermia Induction Device for Hospital Use

Program No. 2004-03

Revision 05, Effective 8-1-04

Contents

1. Product Functional Requirements

1.1 Maintainability Requirements

1.1.1 Operator Maintenance

1. Operational maintenance will be cleaning the condensate collector and external surfaces of the device
2. Preventative maintenance shall include visual inspection of the entire device and cleaning of the ventilation openings
3. Describe operator maintenance and preventative maintenance schedule in the operator's guide.

1.1.2 Customer Support Maintenance

1. There are no customer support maintenance requirements. The operator performs all preventative maintenance.

1.1.3 Verification and Validation

1. Perform verification of Maintainability Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Maintainability Requirements on a Manufacturing Prototype.

1.2 Operational Requirements

1.2.1 Intended Use

1. The device is to be used for the induction of therapeutic hypothermia and hyperthermia that is induced through cooling or heating of blood extra-corporeally by a disposable extra-corporeal circuit and a heat exchanger.
2. The device will be applicable to 95% of the adult population as defined in the AAMI / ANSI HE74-2001 Human factors design process for medical devices.

1.2.2 Physical Description

1. The device will be a stand-alone product with a pump system, heat exchanger, custom electronics, inputs and readout for patient temperature sensors and a disposable extra-corporeal circuit.
2. The device will consist of a durable framed enclosure containing a primary heat exchanger, blood pump, custom electronics and operator interface. A disposable extra-corporeal circuit consisting of a secondary heat exchanger, bubble trap, blood filter, bubble detector, flow meter, pressure sensor, tubing set and connecting means.
3. The device will be movable with wheels for ease of movement such that a single individual can maneuver it.
4. The device weight will be a maximum of 100 kg.
5. The cube dimensions will be a maximum of 21 in W X 45 in H X 25 in D.

1.2.3 Operating Modes

The device will operate in the following modes.

1. Monitor Mode, whereby the system temperature sensor readings are displayed.
2. Patient Cooling Mode, whereby the blood is pumped through the extra-corporeal circuit and the blood temperature is cooled and maintained at a temperature set point determined by the operator input and the device initiates a Maintenance Routine that maintains the preset patient sensor temperature.

3. Patient Heating Mode, whereby the blood is pumped through the extra-corporeal circuit and the blood temperature is heated and maintained at a temperature set point determined by the operator input and the device initiates a Maintenance Routine that maintains the preset patient sensor temperature.

1.2.3.1 Monitor Mode

In this mode, the device will monitor and display temperature sensor readings.

1. The operator will connect the disposable tubing set to the device.
2. The operator will prime the disposable extra corporeal circuit with a sterile solution.
3. The operator will connect the device to the patient via catheters and temperature sensors.
4. All temperature sensor readings are displayed.

1.2.3.2 Patient Cooling Mode

In this mode, the device will pump blood through the disposable extra-corporeal circuit that contains the secondary heat exchanger, and will cool the blood to achieve the patient temperature set point. The following describes the required steps.

1. The operator will input a patient temperature set point.
2. The operator will select the desired flow rate from preset values.
3. The device will cool the blood exiting the heat exchanger and maintain the patient temperature at the selected set point.
4. The device will monitor and display two patient temperatures, blood inflow temperature and blood outflow temperature.
5. The device will alert the operator if a detected fault occurs.

1.2.3.3 Patient Heating Mode

In this mode, the device will pump blood through the disposable extra-corporeal circuit that contains the secondary heat exchanger, and will heat the blood to achieve the patient temperature setpoint. The following describes the required steps.

1. The operator will connect the disposable tubing set to the device.
2. The operator will prime the disposable extra corporeal circuit with a sterile solution.
3. The operator will connect the device to the patient via catheters and temperature sensors.
4. The operator will select the desired flow rate from preset values this action will switch the device to the patient heating mode.
5. The device will adjust the blood temperature exiting the heat exchanger to achieve the patient temperature set point.
6. The device will monitor and display two patient temperatures, blood inflow temperature and blood outflow temperature.
7. The device will alert the operator if a detected fault occurs.

1.2.3.4 Maintenance Routine

During this routine, the device will maintain the patient temperature sensor at an operator-selected set point.

1. The operator will input the desired patient temperature.
2. When the patient temperature monitor detects that the patient temperature has reached the selected temperature the operator will be alerted.
3. The device will switch to the Maintenance Routine and use the feed back from the patient temperature sensor to maintain the patient temperature at the set point.

1.2.4 Operator Interface

1.2.4.1 The operator input interface will consist of a means of selecting the following parameters:

1. Blood flow rate
2. Patient temperature set point

1.2.4.2 The device output to the operator will consist of the following:

1. Device power on/off indicator
2. Read out for patient temperature set point
3. Read out for (2) patient temperature sensors
4. Read out for flow rate set point
5. Read out for inflow and outflow temperatures
6. Elapsed time display for procedure duration
7. Read out for inflow pressure

1.2.5 Training

1. Provide sufficient information in educational materials, labeling, and the operator's guide.

1.2.6 Verification and Validation

1. Perform verification of Operational Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Operational Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

1.3 Quality Requirements

1.3.1 General

1. The manufacturing processes will assure the device is free from defects and meets all product specifications.
2. The quality system used in the design, manufacture, packaging, labeling, storage, installation, and servicing of the device will comply with the applicable requirements of the following:
   - The FDA Quality System Regulation (FDA QSR) as defined in 21CFR, Parts 820, latest revision
   - ISO 13485:2003(E), Medical Devices – Quality management systems – Requirements for regulatory purposes
   - Any other applicable standard or regulation referenced in the FDA QSR or ISO 13485:2003(E).

1.3.2 Verification and Validation

1. Perform verification of Quality Requirements on both the Engineering and Manufacturing Prototypes.
2. Validate the Quality Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

1.4 Repairability Requirements

1.4.1 General

1. Ardiem Medical authorized service centers or factory service personnel will perform all repairs.
2. Design the device to allow easy internal access to perform repairs.
3. Develop a service manual with sufficient detail for a trained service technician to isolate failures.

1.4.2 Verification and Validation

1. Perform verification of Repairability Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Repairability Requirements on a Manufacturing Prototype.

2. Product Performance Requirements

2.1 Durability Requirements

2.1.1 Shock and Vibration

2.1.1.1 Shipping

1. The device will withstand normal levels of vibration for selected modes of transportation as defined in MIL-STD-810F, figure 514.5-1, without incurring functional damage when in the shipping configuration.
2. The device will withstand normal levels of shock for selected test procedures as defined in MIL-STD-810F, Method 516.5, without incurring functional damage when in the shipping configuration.

2.1.1.2 Handling

1. The device will withstand, in the uncrated configuration, hitting walls and other fixed obstacles at a walking speed and moving in and out of elevators and over thresholds at walking speed.

2.1.1.3 Solvents and Fluids

1. All exposed surfaces will be resistant to damage from commonly used hospital/clinical cleaning fluids (such as alcohol and 10% bleach) and contact with salts, bodily fluids, and glucose solutions.

2.1.1.4 RFI and EMI

1. The device will meet the RFI and EMI immunity requirements listed in 2.2.1 1-4

2.1.1.5 Verification and Validation

1. Perform verification of Durability Requirements on Engineering Prototypes at an external test facility. After each test run, perform a functional test to verify the device performance. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Durability Requirements on a Manufacturing Prototype.

2.2 Environmental Requirements

2.2.1 EMC Requirements

1. Electrostatic Discharge Immunity: EN 61000-4-2: 1995 +A1: 1998 +A2: 2001
2. Radiated Electromagnetic Field Immunity: EN 61000-4-3: 2002 +A1: 2002
3. Electrical Fast Transient / Burst Immunity: EN 61000-4-4: 1995 +A1: 2001 +A2: 2001
4. Surge Immunity: EN 61000-4-5: 1995, +A1: 2001
5. Radiated and Conducted Emissions: EN 55011: 1998 +A1: 1999 +A2: 2002, FCC Part 15
6. Power Harmonics, EN 61000-3-2: 2000
7. Voltage Fluctuation (Flicker): EN 61000-3-3: 1995, +A1: 2001
8. Medical Electrical Equipment EMC: EN 60601-1-2: 2001

2.2.2 Operating Requirements

1. Temperature: 20°C to 25°C
2. Humidity: 30% to 75% max non-condensing relative
3. Pressure: 523mm Hg max 10,000 feet altitude

2.2.3 Storage Requirements

1. Storage Temperature: -40°C to 70°C
2. Humidity: 15% to 95% max non-condensing relative
3. Pressure: 179mm Hg max 35,000 feet altitude

2.2.4 Verification and Validation

1. Perform verification of EMC Environmental Requirements on a Manufacturing Prototype at a certified test facility.
2. Perform verification of Operating and Storage Environmental Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
3. Validate the Operating and Storage Environmental Requirements on a Manufacturing Prototype.

2.3 Performance Requirements

2.3.1 Electrical Requirements

2.3.1.1 Electrical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with UL 60601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety.
2. Use relevant components that are approved by at least one agency.

2.3.1.2 Power

1. Use a power cord that is tested and certified to meet European Community electrical safety requirements for EU approval.
2. Use a power cord that is tested and certified to meet United States electrical safety requirements for FDA approval.
3. Fuse each side of the mains.
4. Line Voltage: 115 VAC +/-10% or 230 VAC +/-10%.
5. Line Current: 20 A maximum.
6. Line Frequency: 60 Hz +/- 3% or 50 Hz +/-3%.
7.

2.3.1.3 Verification and Validation

1. Perform verification of Electrical Safety Requirements on a Manufacturing Prototype at an external test facility. Perform verification of all other applicable Electrical Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Electrical Requirements on a Manufacturing Prototype.

2.3.2 Electronic Requirements

2.3.2.1 Central Processing Unit

1. Use a central processing unit (CPU) to control the overall operation of the device, including data acquisition, electro-mechanical components, operator interfaces, and communications interfaces.
2. Provide capability to reset CPU without cycling power off and on.

2.3.2.2 Real-Time Clock

1. Maintain the device's total operation time over its life.

2. Use a real-time clock (RTC) to associate a specific date and time with each reported measurement.
3. The RTC will continue to operate in the absence of AC line power.

2.3.2.3 PCBAs

1. Design device with no more than three (3) PCBAs.

2.3.2.4 Operator input

The operator will input the following data:

1. Power on/off will be initiated by a switch
2. The blood flow rate will be entered, on a touch-screen display, from preset values between 200mL/min and 900 mL/min in 100 mL/min increments.
3. Patient temperature set point will be selected and indicated on a touch-screen display. The set points will be 30°C, 34°C and 37°C.

2.3.2.5 Operator output

The following data will be output from the device:

1. Power on will be indicated by a lighted rocker switch
2. The blood inflow and outflow temperatures will be indicated on the touch-screen display. A status indicator will
3. The blood flow rate will be indicated on the touch-screen display. The device will maintain the pre-set flow rate within ±10% for any selected flow rate.
4. The patient temperature readout accuracy will be ±0.2°C over the range of 30°C to 37°C.
5. The patient temperature control will be maintained to within ±0.5°C
6. An audible alarm and warning indicator on the touch-screen display will indicate when a device fault has been detected.

2.3.2.6 Safety limits

1. The electronics hardware limit will detect and shut down the pump and primary heat exchanger if the secondary heat exchanger temperature (inflow) drops below 5°C or rises above 41°C.
2. The device will activate an occluding mechanism in the tubing set and shut down the pump if the bubble detector verifies the presence of any bubbles larger than 20µl in the tubing set after the blood filter and display a warning message on the touch-screen display

2.3.2.7 Verification and Validation

1. Perform verification of Electronic Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Electronic Requirements on a Manufacturing Prototype.

2.3.3 Embedded Software Functional Requirements

2.3.3.1 General

1. Control system operation.
2. Invoke operator input.
3. Provide output.
4. Monitor and control temperatures.
5. Monitor and control flow rate.
6. Monitor inflow pressure.

7. Monitor procedure elapsed time.

2.3.3.2 Data Collection, Processing, and Relaying

1. Acquire temperatures, flow rate, flow pressure and elapsed time.
2. Compute averages.
3. Display average temperatures.
4. Report all averages over a serial link.

2.3.3.3 Test and Diagnostics

1. Perform tests to detect faults.
2. Display faults using messages on a touch-screen display.
3. Alert operator by sounding an audible alarm.

2.3.3.4 Safety limits

1. The software will detect if the inflow temperature drops below 5.5°C or rises above 40.5°C and display a warning message.
2. The software will detect if the primary heat exchanger temperature drops below 2°C or rises above 42°C and display a warning message.
3. The software will detect the presence of bubbles within the inflow tubing and display a warning message.

2.3.3.5 Verification and Validation

1. Perform verification of Embedded Software Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Embedded Software Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

2.3.4 Mechanical Requirements

2.3.4.1 Mechanical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with the mechanical safety requirements of UL 60601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety. Also, design and manufacture the device to comply with safety requirements for specific components or systems, such as refrigerating systems (ISO 5149:1993 Mechanical refrigerating systems used for cooling and heating – Safety requirements, and ASHRAE Standard 15-2001 – Safety Standard for Refrigeration Systems), fan guarding (ISO 12499:1999 Industrial fans – Mechanical safety of fans – Guarding), and electromechanical relays (IEC 61810-1:2003 Elementary relays -- Part 1: Safety and general requirements).

2.3.4.2 Thermal Requirements

1. Isolate the electrical/electronics compartment from the refrigeration compartment.
2. Limit the internal device temperature to 40°C under normal operating conditions.

2.3.4.3 Verification and Validation

1. Perform verification of Safety Requirements on a Manufacturing Prototype at an external test facility.

2. Perform verification of other Mechanical Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.

3. Validate the Mechanical Requirements on a Manufacturing Prototype.

2.4 Reliability Requirements

1. Useful service life is five years with normal servicing and maintenance.

2. Perform verification of Reliability Requirements on Manufacturing Prototypes by analysis based on MIL STD 217.

2.5 Safety Risk Management Requirements

2.5.1 Safety Modes

For purposes of evaluating risk and determining the proper performance of failure detection and safety in the design, safe operation is defined as one of the following:

1. The ability to detect fault conditions and alert the operator constitutes the primary safety mode of the system.

2. The ability to detect a threatening condition and alert the operator constitutes the secondary safety mode of the system.

3. The tertiary safety mode will be to shut down the pump and heating or cooling cycle.

2.5.2 General Risks

1. Identify undesirable system operating conditions with a system risk analysis. The design will anticipate, to the extent possible, the occurrence of failure modes and provide a means of protecting against them. (EN ISO 14971:2000 Medical devices – Application of risk management to medical devices)

2. General surgical procedural risks, those common to all surgical procedures, are outside the boundaries of the risk assessment for this device.

3. Evaluate risk per EN ISO 14971:2000 Medical devices – Application of risk management to medical devices .

4. Instructions and labeling must fulfill requirements of: FDA Title 21 CFR Part 801 Labeling; MDD 93/42/ EEC, Annex 1, Essential Requirements; EN 1041 Information supplied by the manufacturer with medical devices; EN 980+A1 Graphical symbols for use in the labelling of medical devices ; and requirements of Ardiem Medical material handling and quality procedures.

5. Include adequate operator safety instructions in manuals and labeling supplied with the device.

2.5.3 Verification and Validation

1. Perform verification of Safety Risk Management Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.

2. Validate the Safety Risk Management Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

3. Product Interface Requirements

3.1 Customer Interface Requirements

3.1.1 General

1. Provide appropriate instructional materials (operator's guide, training video, screen prompts, etc.) to allow operator to correctly install and use the device.

3.1.2 Buzzer

1. Use an audible alarm to prompt and/or alert the operator when a failure has occurred and/or an action is required.

3.1.3 Display

1. The device will contain a touch-screen display capable of displaying procedure data and device status.
2. The display will be readable under all ambient light conditions.
3. The device will display temperatures, flow rate, inflow pressure, elapsed time, error messages, messages, etc. to the operator for communicating to a service technician.

3.1.4 Controls

1. Include touch-screen software to allow the operator to select blood flow rate set point.
2. Include touch-screen software to allow the operator to select a patient temperature set point.
3. Control panel to include a large push-button switch to deactivate pump motor.

3.1.5 Language

1. Allow factory configuration to a minimum of one language out of supported languages.
2. Include the following supported languages as a minimum: English (U.S.)
3. Use symbols in accordance with EN 980.

3.1.6 Units of Measure

1. Label controls and display selected and measured values in the following units of measure:
   - Flow rate: milliliters per minute (mL/min)
   - Temperature: degrees centigrade (°C)
   - Pressure: millimeters of mercury (mmHg)
   - Time: minutes (min)

3.1.7 Verification and Validation

1. Perform verification of Customer Interface Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Customer Interface Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

3.2 External Interface Requirements

3.2.1 General

1. The device will contain a serial port capable of communications with a computer (diagnostics only).
2. Use a RS-232 with a DB-9 connector as the serial port electrical interface.
3. Use serial port communications at a minimum baud rate of 19200 baud.

3.2.2 Verification and Validation

1. Perform verification of External Interface Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the External Interface Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

3.3 Labeling Requirements

3.3.1 General

1. Manuals and labels will conform to both European Community (93/42/EEC MDD) and FDA (Title 21 CFR 801) requirements.
2. All labels and manuals will comply with requirements of EN 1041, EN 980, and any other applicable standards.
3. Labeling will also contain the following wording prominently displayed: "CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician."

3.3.2 Safety and Warning Labels

1. Provide adequate safety labels per 93/42/EEC MDD, Title 21 CFR 801, EN 1041, and EN 980.
2. Identify and explain any warnings in the operator's guide.

3.3.3 Shipping Labels

1. TBD

3.3.4 Verification and Validation

1. Perform verification of Labeling Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Labeling Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

3.4 Service Delivery Requirements

3.4.1 General

1. Deliver all necessary information and support products with the main product delivery.
2. A training program will be available for training of repair and maintenance personnel.
3. Provide a system for supplying spare modules to repair and maintenance personnel.

3.4.2 Verification and Validation

1. Perform verification of Service Delivery Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.

2. Validate the Service Delivery Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

4. Revisions

Rev.	Description	Author	Effective Date
00	Preliminary Issue	Ralph Gill	9/26/02
01	Completed Requirements	Mike Pitsakis	9/19/03
02	Updated references to industry regulation and standards	Joseph Klingensmith	10/02/03
03	General revisions to specifications	Mike Pitsakis	02/05/04
04	General revisions to specifications, changed program number from 2003-01 to 2004-03	Bill Novak	03/19/04
05	Added 4.4.1.2	Mike Pitsakis	08/02/04

Appendix H

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00018

TITLE OF TECHNICAL REPORT		REVISION
Current Draw of Hypothermia Induction Devices and Effect on Portability		00
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-03	6/22/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT		NAME OF AUTHOR
Electrical power requirements and limitations		Mike Pitsakis

TECHNICAL AREA

Current measurements

SUBJECT AND KEY TECHNICAL WORDS

Current measurements

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

TR_Hypo 030708 MP.doc, TR Hypo 020727 CR.doc

Abstract

Current drawn from the line and from the DC power supply were measured on both Mild-Moderate device engineering prototypes and both Profound device engineering prototypes. The refined Mild-Moderate Prototype 2 draws 16.9 A in full operation which is below the set limit of 20 A. This allows for the additional draw of a touch-screen and single board computer that are planned to be incorporated in the clinical prototype of the ER device. However, the device, due to electrical power requirements, is not adaptable for battery operation and can only be used in large emergency vehicles that provide 120 VAC. The Profound devices, Engineering Prototype 1 and 2, draw 0.84 A from the line and also allow use of a touch-screen and a single board computer for graphical user interface. Battery operation, at a 5 A draw on a portable version of a profound device, merely involves only repackaging.

Background

In a previous technical report titled "Hypothermia Induction Devices Electrical Power Requirements", TR_Hypo 030708 MP.doc, Power requirements for the Mild-Moderate and Profound Hypothermia Induction Devices were estimated based on manufacturer data. The possibility of device transition to portable battery operation was also discussed.

Introduction

Excessive current draw of the Hypothermia Induction devices presents an obstacle to portability. After constructing two Mild-Moderate device engineering prototypes and two Profound device engineering prototypes, we measured current that was drawn from the line and from the DC power supply

Purpose

Current draw data is reported here as well as conclusions regarding portability that resulted from these measurements.

Description of Apparatus and Setup

Current draw from the line was measured inductively using a Wavetek Meterman model AC40A and repeated by measuring the voltage drop in a 0.1 W resistor connected in series with the hot wire using a Fluke Multimeter model 23III set for AC voltage. Current draw from the DC power supply was measured using a Fluke Multimeter model 23III set for DC voltage.

Summary of Data and Results

Current draw by the motor of the pump in all prototypes depends on flow rate as shown in the table in Figure 1. Flow rates of 900mL/min and 2000mL/min are maximum values for Mild-Moderate and Profound devices respectively. There is a transient surge on start up.

Mild-Mod 12 VDC Pump Motor at flow (mL/min)	Profound 12 VDC Pump Motor at flow (mL/min)	Current Drawn from line (A)	Current Drawn from line at start up (A)
200	500	0.06	0.20
500	1000	0.11	0.50
900	2000	0.14	0.70

FIGURE 1

Current Drawn by the individual components of Mild-Moderate device Engineering Prototype 1 is summarized in the table shown in Figure 2. It includes pump motor current at maximum flow rate and totals for heater and no heater operation. For heater operation the total exceeds the maximum draw set for 20 A.

Eng. Prototype 1	Current Drawn from line (A)	Current Drawn from line at start up (A)
Power Supply/Fan	0.20	0.20
Electronics	0.05	0.05
Pump at 900mL/min	0.14	0.70
Compressor	15.70	16.50
Heater	7.00	7.00
Total w/o heater	16.09	17.45
Total w/ heater	22.89	24.25

FIGURE 2

Current Drawn by the individual components of the refined Mild-Moderate device Engineering Prototype 2 is summarized in the table shown in Figure 3. It includes pump motor current at maximum flow rate and totals including heater. This prototype is optimized for operation below the maximum draw set for 20 A.

Eng. Prototype 2	Current Drawn from line (A)	Current Drawn from line at start up (A)
Power Supply/Fan	0.20	0.20
Electronics	0.05	0.05
Pump at 900mL/min	0.14	0.70
Compressor	9.80	11.30
Heater	6.00	6.00
Total	16.19	18.25

FIGURE 3

Current Drawn by the individual components of both Profound device Engineering Prototype 1 and 2 is summarized in the table shown in Figure 4. It includes pump motor current at maximum flow rate. This device draws less than 1 A from the line while for 12 VDC operation it requires less than 9 A.

Eng. Prototype 1&2	Current Drawn from line (A)	Current Drawn from 12V Power Supply (A)
Power Supply/Fan	0.28	2.80
Electronics	0.05	0.50
Pump at 2 L/min	0.14	1.40
Compressor	0.37	3.70
Total	0.84	8.40

FIGURE 4

Note that the switching power supply consumes 2 A for its own operation and for the minimum load while the blower fan consumes 0.8 A.

Conclusions

The refined Mild-Moderate Prototype 2 show s current draw that is well below the limit for operation in a hospital ER or OR and leaves room for additional draw of a touch-screen and a single board computer. However this is excessive for ambulance vehicles except for larger ones that have 120VAC/2000 VA generators (see technical report titled "Electrical Power for Portable Hypothermia Devices", TR_Hypo 020727 CR.doc).

The Profound Prototypes 1 and 2 draw a small amount of current from the line, which leads to no problems of adding a touch-screen and a single board computer in the clinical prototype of the ER unit. Correspondingly it draws a moderate amount from 12 VDC that lends the unit to portability. Therefore repackaging the unit and replacing the 12 VDC power supply by a battery easily adapts the unit for emergency vehicle use. As a matter of fact, since there will be no power supply, the total current draw will be 5 A. Now since there is no need for the pump and compressor to be on at the same time this will reduce the battery requirements to 5 A which will also reduce battery size and weight.

In general actual current draw is less than was estimated because maximum values reported by the manufacturers were used in conservative estimates.

Suggestions for Further Work

Current draw measurements must be repeated in Clinical Prototypes of Mild-Moderate and Profound Hypothermia Induction device prototypes.

Appendix I

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00026

TITLE OF TECHNICAL REPORT		REVISION
CO_2 Cooling Capability for Mild-Moderate and Profound Hypothermia Devices		0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Emergency Hypothermia	2004-03	08/31/2004
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Alternate cooling methods	Doug Schendel	

TECHNICAL AREA

Thermodynamics, Heat Transfer, Fluid Dynamics

SUBJECT AND KEY TECHNICAL WORDS

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	X Other

ASSOCIATED REPORTS

TR_Hypo 030606 MP.doc, TR_Hypo 020822 RG.doc, TR_Hypo 020205 RG.doc, TR_Hypo 031205 MP.doc, TR_Hypo 031205 MP.doc, Blood Shunt Cooling Calcs.doc, Liquid CO2 Heat Exchanger.doc,

Average Properties of Blood and Human Body.doc

Abstract

This technical report presents an investigation of the feasibility of inducing Mild-Moderate Hypothermia (average body core temperature of 30-34 °C) and Profound Hypothermia (average body core temperature of 10-20 °C) using compressed liquid CO_2 (carbon dioxide) as the cooling source. The advantage of CO_2 cooling over the standard mechanical vapor-compression (refrigeration) is its applicability to emergency medical vehicle use and in-field use without the need for electrical outlet power.

When liquid CO_2 is passed through a pressure-dropping orifice to near-atmosphere conditions, a cold combination of gas and solid dry ice particles are discharged in a high velocity jet. The cold discharge temperature (between -70 °F and -109 °F, depending on orifice geometry) results from the CO_2 phase change from saturated liquid to superheated vapor. The cold CO_2 is piped directly into the primary side of a heat exchanger, identical to the nonportable Mild-Moderate hypothermia heat exchanger, using mechanical vapor-compression for the cooling source.

Test results show CO_2 cooling to be an easily controlled, perfectly adequate alternative to mechanical vapor-compression cooling and having the additional quality of portability since no electrical outlet power is required.

Background

Standard mechanical vapor-compression cooling has been successfully used to cool blood flow and thus lower average body core temperature to induce Mild-Moderate hypothermia. Profound hypothermia is ordinarily induced by a cold flush from 10-20 L of prechilled fluid, necessitating the need for additional refrigeration. Since mechanical vapor-compression equipment is heavy and unwieldy, an alternative cooling source was needed for applicability to emergency medical vehicles and in-field applications.

Introduction

Due to its portability and lack of need for electrical outlet power, liquid CO_2 cooling was investigated as the cooling source to induce both Mild-Moderate and Profound states of hypothermia.

Purpose

The purpose of this investigation is to determine if liquid CO_2 cooling can adequately cool blood flow to induce both Mild-Moderate and Profound states of hypothermia for use in emergency medical vehicles and in-field applications

Description of Apparatus and Setup

Water was used as the cooling medium for both the Mild-Moderate and Profound hypothermia investigations due to similar thermophysical and transport properties compared to blood as shown in **Table 1** below. Ambient test conditions for both investigations were 74 °F (23.3 °C) and 14.7 psia.

Table 1 - Thermophysical and Transport Properties of Blood and Water

Thermo Property	Blood	Water
Density, ρ	1060 kg/m^3 = 66.17 lbm/ft^3	1002 kg/m^3 = 62.57 lbm/ft^3
Specific Heat, C_p	3.8 kJ/(kg-°C) = .91 BTU/(lbm-°F)	4.22 kJ/(kg-°C) = 1.01 BTU/(lbm-°F)
Thermal Conductivity, k	.492 W/(m-°C) = .284 BTU/(hr-ft-°F)	.552 W/(m-°C) = .319 BTU/(hr-ft-°F)
Thermal Diffusivity, α	1.22E-7 m^2/s = 4.73E-3 ft^2/hr	1.31E-7 m^2/s = 5.06E-3 ft^2/hr

Compressed liquid CO_2 is stored in specially designed, portable containers. Each filled container holds part liquid and part gaseous CO_2 in the saturated state. Containers used for CO_2 cooling MUST possess a "siphon tube" so liquid CO_2 is drawn from the container's bottom, as opposed to the gaseous CO_2 above the liquid. Several 20 lb containers (net CO_2 weight) were the CO_2 source for these investigations.

Liquid CO_2 discharging from the 20 lb containers flowed first through an electric solenoid valve, which was used to manually control fluid temperature exiting the secondary side of the heat exchanger. The target temperature for this flow (patient inflow) was 6-10 °C. Whenever the solenoid valve was opened, liquid CO_2 was fed through precision orifice(s) and expanded to near-atmospheric pressure in the expansion manifold. The Mild-Moderate investigation used a single orifice and the Profound investigation used both a single and double orifice. Each orifice had a flow diameter of .020 inches. The expanded, and thus cold, CO_2 was then immediately fed into the primary side of the heat exchanger. Warmer CO_2 exiting the heat exchanger was discharged to the outside atmosphere through several feet of 1 inch diameter hosing.

The Mild-Moderate hypothermia investigation used a shunt flow arrangement that circulated fluid through a high surface-area fluid bag in direct physical contact with the secondary side of the heat exchanger. The cooled fluid mixed with a larger fluid reservoir (Pig Simulator -- see Technical Report TR_Hypo 031205 MP.doc) which simulated the cardiovascular system of a 25 kg pig. Flow rate through the common mixing tube was 2 L/min with .5 L/min flowing through the heat exchanger and 1.5 L/min flowing through the Pig Simulator. A schematic view of the test apparatus for the Mild-Moderate case is shown in **Figure 1** on the following page. Temperatures were recorded every 3 seconds for Ambient, Outflow (outflow of patient is flow into heat exchanger), Inflow (inflow of patient is flow out from heat exchanger), Evaporator (heat exchanger plates), Patient 1 (Pig Simulator body core #1) and Patient 2 (Pig Simulator body core #2). All temperature results are shown plotted versus time (minutes) in **Figure 3**.

The Profound hypothermia investigation simply pumped fluid from a 20 L bag (at ambient conditions) through the secondary side of the heat exchanger at varying flow rates of 1.5-2 L/min. The cooled fluid was meant for infusion directly into the patient but was discharged to the indoor atmosphere for this investigation. Due to the higher Profound flow rates, part of this investigation used a double orifice arrangement. A schematic view of the test apparatus for the Profound case is shown in **Figure 2** on the following page. Temperatures were recorded every 3 seconds for Ambient, Outflow, Inflow,

Evaporator and Fluid Bag. All temperature results are shown plotted versus time (minutes) in **Figures 4-7** for various combinations of orifices and flow rates.

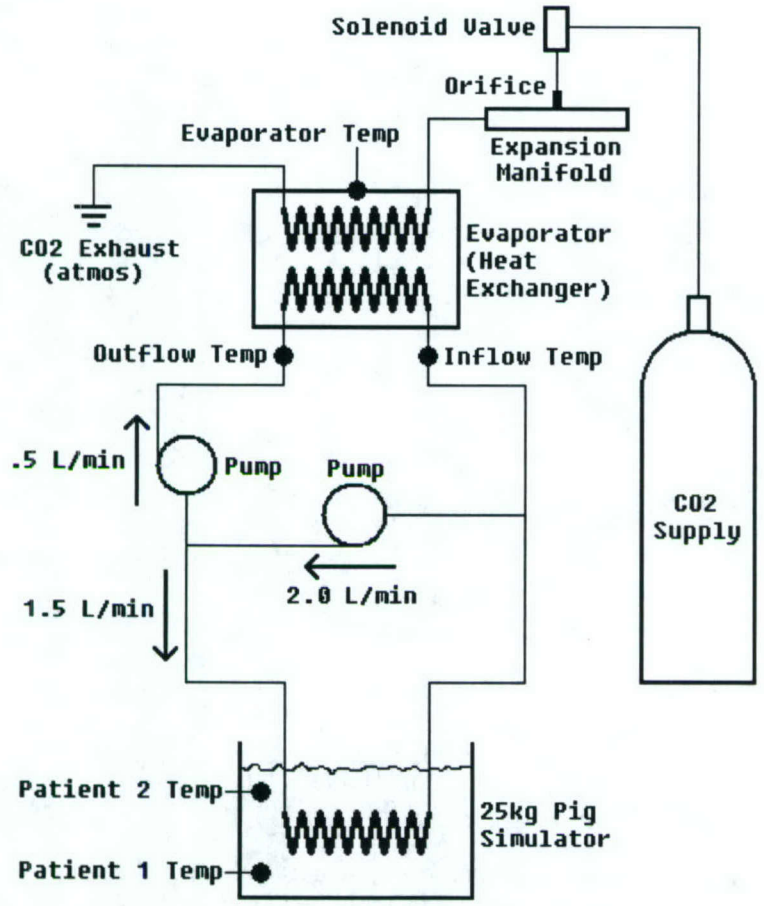


Figure 1 – Test Apparatus for Mild-Moderate Hypothermia

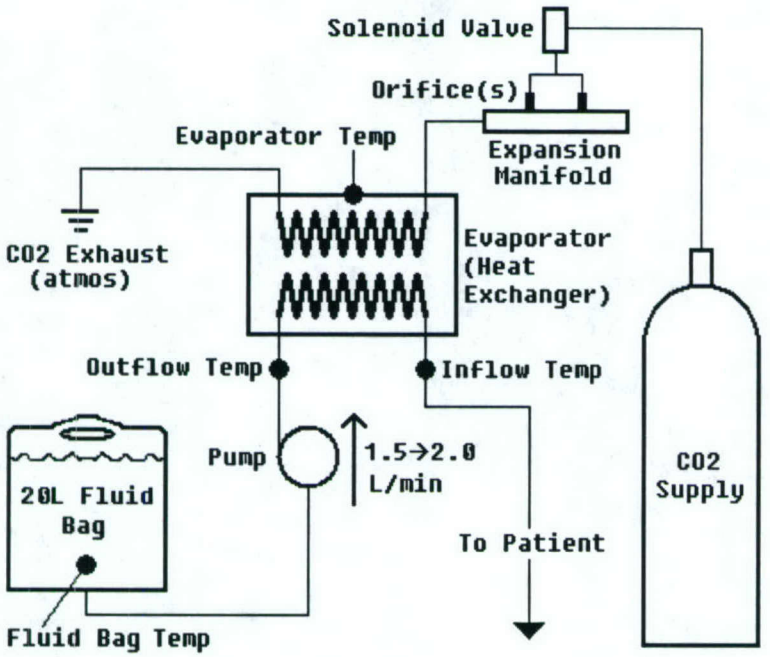


Figure 2 – Test Apparatus for Profound Hypothermia

CO_2 Flow

Flow of liquid CO_2 through an orifice to atmosphere or near-atmospheric conditions is an extremely complex phenomenon. The orifice discharge will be part CO_2 gas and part CO_2 "snow" (solid dry ice particles). As the pressure drops in the orifice, gas bubbles form and the percentage of gas increases. As pressure drops below the triple point of 75.12 psia, the remaining liquid changes into a solid. Thus the flow is multiphase and compressible. However, to compute a rough mass flow approximation through the orifice, or to size an orifice for existing conditions, the following procedure can be applied:

Orifice Inlet Conditions:
Liquid CO_2
Tin = 70 °F
Pin = 853 psia = CO_2 vaporization pressure @ 70 °F

Assuming an isenthalpic pressure drop to the triple point, the flow would consist of approximately 48% by mass of "snow" and 52% by mass of gas. In this state the density of the "snow" is 73.5 lbm/ft^3 and the gas is .875 lbm/ft^3. The nozzle discharge in % by volume is:

Volume Snow / Volume Gas = (Mass Snow/Density Snow) / (Mass Gas/Density Gas)
= (.48 * Mass Total/Density Snow) / (.52 * Mass Total /Density Gas)
= (.48 * Density Gas) / (.52 * Density Snow)
= (.48 * .875) / (.52 * 73.5)
= .011

and

Volume Snow / Volume Total = Volume Snow / (Volume Snow + Volume Gas)
= Volume Snow / (Volume Snow + Volume Snow / .011)
= 1.0 / (1.0 + 1.0 / .011)
= .0109

As the above shows, the % by volume of snow through the orifice is quite low compared to gas, thus it is reasonable to assume the flow to be gaseous with entrained snow. Additionally, since flow density is expected to vary significantly, the analysis must take into account compressibility effects. The stagnation properties will be the CO_2 container properties:

Stagnation Properties:
T_0 = stagnation temperature = 70 °F
P_0 = stagnation pressure = 853 psia
ρ_0 = stagnation density = 12.7 lbm/ft^3

The equations below govern the flow of compressible fluids and were derived assuming reversible, adiabatic, 1-D steady flow of an ideal gas. Some, but not all, of these assumptions are valid for liquid CO_2 flow through an orifice and sudden expansion to near-atmospheric conditions. However, as stated above, this calculation is used only to acquire a rough approximation of the mass flow through each orifice.

$$\frac{T_0}{T} = 1 + (k-1)\cdot\frac{M^2}{2}$$

$$\frac{P_0}{P} = \left[1 + (k-1)\cdot\frac{M^2}{2}\right]^{\frac{k}{(k-1)}}$$

$$\frac{\rho_0}{\rho} = \left[1 + (k-1)\cdot\frac{M^2}{2}\right]^{\frac{1}{(k-1)}}$$

where: k = CO_2 ratio of specific heats = 1.289
M = Mach number

To see if the flow through the orifice is choked, pressure at the exit plane of the orifice, P*, will be computed assuming sonic velocity (M = 1). If the orifice exit pressure, P_e, is greater than the back pressure condition in the expansion manifold, then sonic velocity exists at the orifice discharge:

$$\frac{P_0}{P_e} = \left[1 + \frac{(k-1)}{2}\right]^{\frac{k}{(k-1)}} = \left[1 + \frac{(1.289-1)}{2}\right]^{\frac{1.289}{(1.289-1)}} = 1.826$$

$P_e = 853 / 1.826 = 467.1$ psia

Since P_e is greater than the manifold back pressure of approximately 40 psia, the orifice discharge velocity is sonic.

Computing temperature and density at the orifice discharge is shown below:

$$\frac{T_0}{T_e} = \frac{(k+1)}{2} = \frac{(1.289+1)}{2} = 1.145$$

$T_e = (70 + 460) / 1.145 = 462.9$ °R = 2.88 °F

$$\frac{\rho_0}{\rho_e} = \left[\frac{(k+1)}{2}\right]^{\frac{1}{(k-1)}} = \left[\frac{(1.289+1)}{2}\right]^{\frac{1}{(1.289-1)}} = 1.595$$

$\rho_e = 12.7 / 1.595 = 7.96$ lbm/ft^3

Computing the orifice sonic velocity, a_e, is now possible since the orifice exit temperature is known. Converted to metric aids in this calculation to make sure all units are handled correctly:

$a_e = \sqrt{k \cdot R \cdot T}$

where: k = 1.289 (dimensionless)
R_{CO2} = .1889 kJ/(kg-°C) = 188.9 J/(kg-K)
T = T_e = 2.88 °F = -16.18 °C = 257.0 K

$a_e = \sqrt{(1.289) \cdot (188.9) \cdot (257.0)}$

= 250.2 m/s = 820.2 ft/s

The mass flow through the orifice can now be computed since the orifice density, mean velocity and flow area are all known.

Mass flow = ρ_e * a_e * Area

where: ρ_e = 7.96 lbm/ft^3
a_e = 820 ft/s
Area = orifice discharge area = 3.14E-4 in^2 (.020 inch diameter)
= 2.18E-6 ft^2

Mass flow = 7.96 * 820 * 2.18E-6

= .0142 lbm/s = .854 lbm/min

The above computed mass flow is very close to the actual observed mass flow rate of 1 lbm/min per orifice.

Recall the above compressible flow calculation assumes adiabatic (no heat transfer to/from environment), reversible (frictionless, nonturbulent), 1-D, steady flow of an ideal gas. Few of these conditions are actually met, yet the calculation is fairly accurate. Thus the above calculation can be used for:

- determining whether orifice discharge velocity is sonic or subsonic
- computing orifice discharge pressure, velocity and density
- sizing orifices to meet required flow rates (to meet required heat transfer rates)

CO_2 Power

From previous investigations and technical reports, at a flow rate of .5 L/min through the secondary side of the heat exchanger, the cooling rate required to lower the core body temperature from 37 °C (98.6 °F) to 34 °C and inlet blood temperature (exiting the secondary side of the heat exchanger) from 37 °C (98.6 °F) to 6 °C ranged between 1000 W - 1300 W.

As mentioned previously, approximately 48% of the CO_2 by mass exits the orifice (and enters the heat exchanger) as solid dry ice and the remaining 52% by mass exits the orifice as CO_2 vapor. Assuming a maximum temperature the CO_2 mix can achieve upon exiting the primary side of the heat exchanger is 6 °, the approximate CO_2 heating rate is:

Mass flow (solid CO_2) = .48 * 1lbm/min = .48 lbm/min

Mass flow (vapor CO_2) = .52 * 1lbm/min = .52 lbm/min

Again assuming an isenthalpic pressure drop through the orifice (orifice calculations above also assumed isentropic flow through orifice – either can be assumed to simplify various calculations but both can't be true for the same flow. In reality, neither is true but the resulting insight and approximate solutions justify the assumption and is standard practice in fluid mechanics, especially for problems involving compressible flow), and with the aid of thermodynamic tables for CO_2, the resulting enthalpy changes are computed between the initial and final states:

Solid CO_2: $h_{initial}$ = 112 BTU/lbm (saturated liquid in container at 70 °F and 853 psia)
Vapor CO_2: $h_{initial}$ = 174 BTU/lbm (saturated vapor in container at 70 °F and 853 psia)
Mix CO_2: h_{final} = 211 BTU/lbm (superheated vapor leaving heat exchanger at 6 °C = 43 °Fand 14.7 psia)

Enthalpy change (solid CO_2) = h_{final} - $h_{initial}$ = 211 – 112 = 99 BTU/lbm

Enthalpy change (vapor CO_2) = h_{final} - $h_{initial}$ = 211 – 174 = 37 BTU/lbm

Total CO_2 heating rate = .48 lbm/min * 99 BTU/lbm + .52 lbm/min * 37 BTU/lbm

= 48 BTU/min + 19 BTU/min = 67 BTU/min = 4020 BTU/hr = 1178 W

As the above calculation shows, enough energy exists in liquid CO_2 to perform Mild-Moderate hypothermia with a single .020-inch diameter orifice. Using 2 orifices should double the blood cooling rate, however, CO_2 consumption would also double.

Summary of Data and Results

Orifice Diameter: .020 inches each

CO_2 Mass Flow per orifice: 1 lb/min

Expansion Manifold Pressure:
$P_{manifold}$ (1 orifice): 12-16 psig
$P_{manifold}$ (2 orifices): 30-40 psig

Expansion Manifold Temperature:
$T_{manifold}$ (1 orifice): -58 °F to –82 °F
$T_{manifold}$ (2 orifices): -62 °F to –92 °F

For the Mild-Moderate case shown in **Figure 3** below, liquid CO_2 cooling had good results, meeting all criteria of 30-34 °C average core body temperature and 6-10 °C patient inflow temperature. Evaporator and patient inflow cool down times were noticeably shorter at 8 °C/min and 6.7 °C/min, respectively, compared to mechanical vapor-compression cooling of

approximately 1 °C/min. This is due primarily to the colder evaporator temperatures attainable with CO_2 cooling. Average core cool down times were very comparable at 0.4 °C/min compared to 0.5 °C/min for mechanical vapor-compression cooling (see technical report TR_Hypo 031205 MP.doc). The rate of cooling of the patient (pig simulator in this case) was quite fast 0.316 °C/min. CO_2 consumption was 8 lbs to cool the patient to 34°C (half of this amount was consumed before the patient temperature started dropping) and an additional 3.5 lbs to cool to 30°C.

For the Profound pre-cooling of the Evaporator – the no flow case (no flow through secondary side of heat exchanger) shown in **Figure 4** below, the liquid CO_2 cooling had slightly better results than the Mild-Moderate case above at 12 °C/min. This is expected since the Mild-Moderate case had a flow of 500 ml/min in the secondary side of the heat exchanger during evaporator cool down.

For the Profound case with single orifice at 2 L/min shown in **Figure 5** below, liquid CO_2 cooling with a single orifice could not reduce patient inflow to 6-10 °C. This was due to 4 times the volumetric flow rate compared to Mild-Moderate. Surprisingly, the delta T between patient outflow and inflow was a good 12 °C compared to 17 °C for Mild-Moderate. However, outflow temperature was cooler than Mild-Moderate.

For the Profound case with double orifice at 2 L/min shown in **Figure 6** below, liquid CO_2 cooling with a double orifice, if allowed to continue a few more minutes, would have attained the 6-10 °C inflow temperature requirement. This was due to doubling the CO_2 mass flow. The delta T between patient outflow and inflow was 16 °C, compared to 12 °C for the Profound single orifice @ 2 L/min and 17 °C for the Mild-Moderate.

For the Profound case with double orifice at 1.5 L/min shown in **Figure 7** below, liquid CO_2 cooling definitely was able to attain the 6-10 °C inflow temperature, as expected. This was due to slightly lower volumetric flow rate through the secondary side of the heat exchanger. The delta T between patient outflow and inflow was 19 °C compared to 16 °C for Profound double orifice @ 2 L/min and 12 °C, for Profound single orifice @ 2 L/min, and 17 °C for Mild-Moderate.

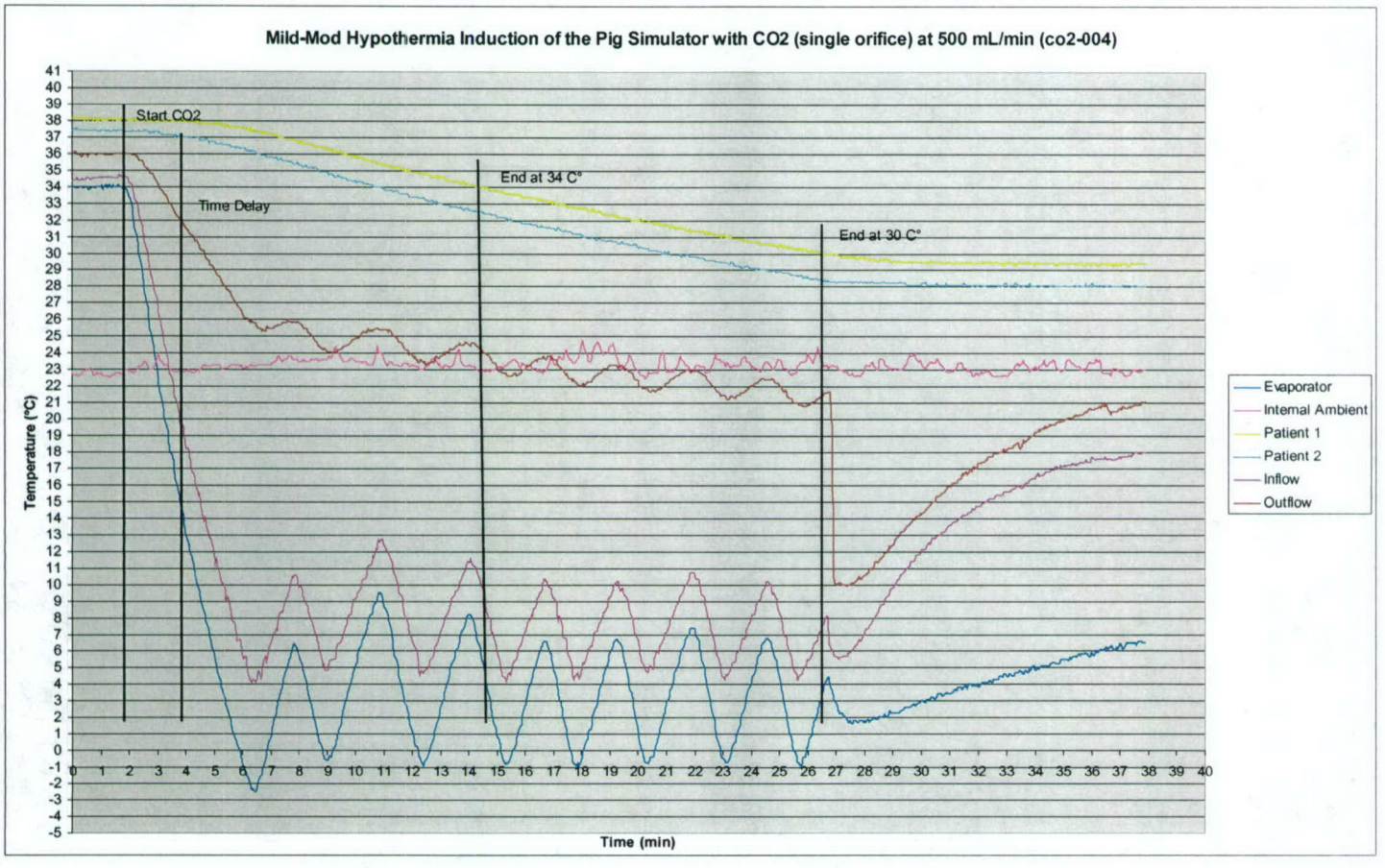
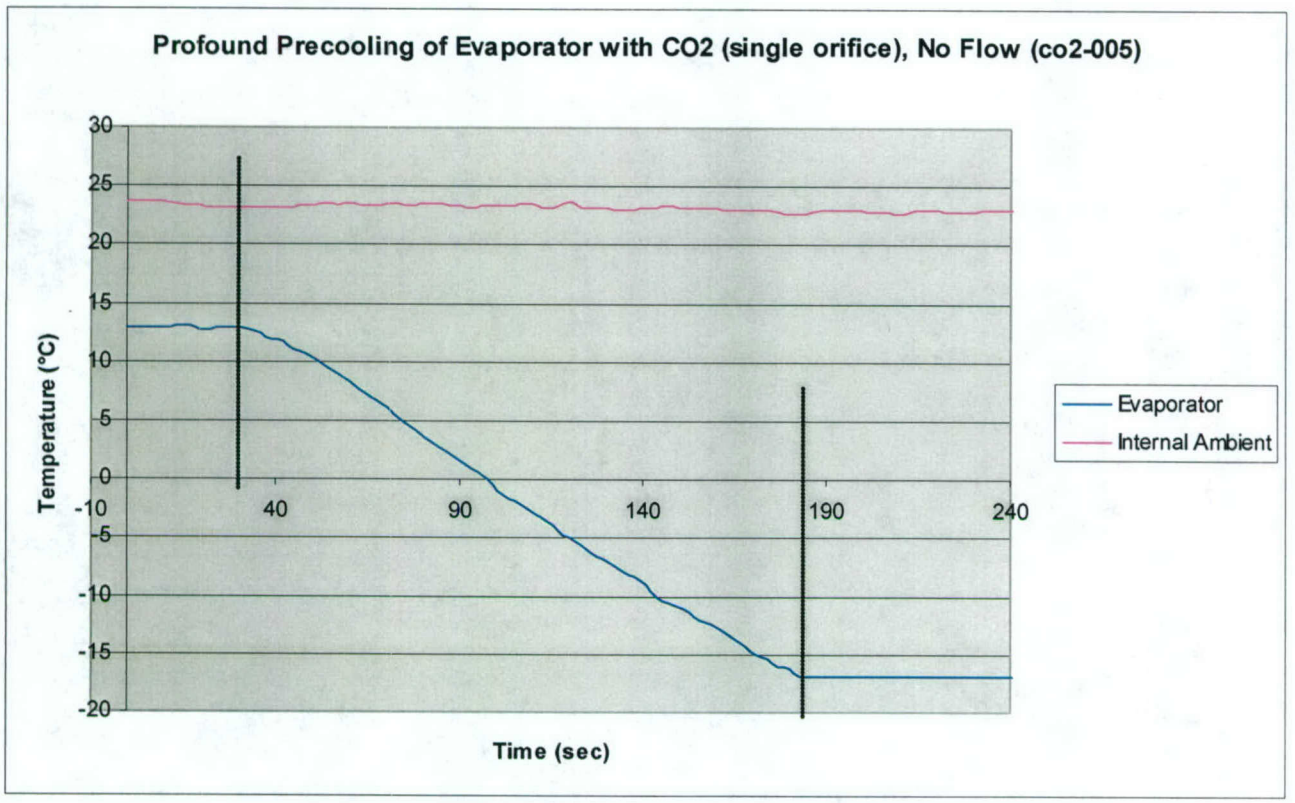


Figure 3 – Temperature Results for Mild-Moderate Hypothermia



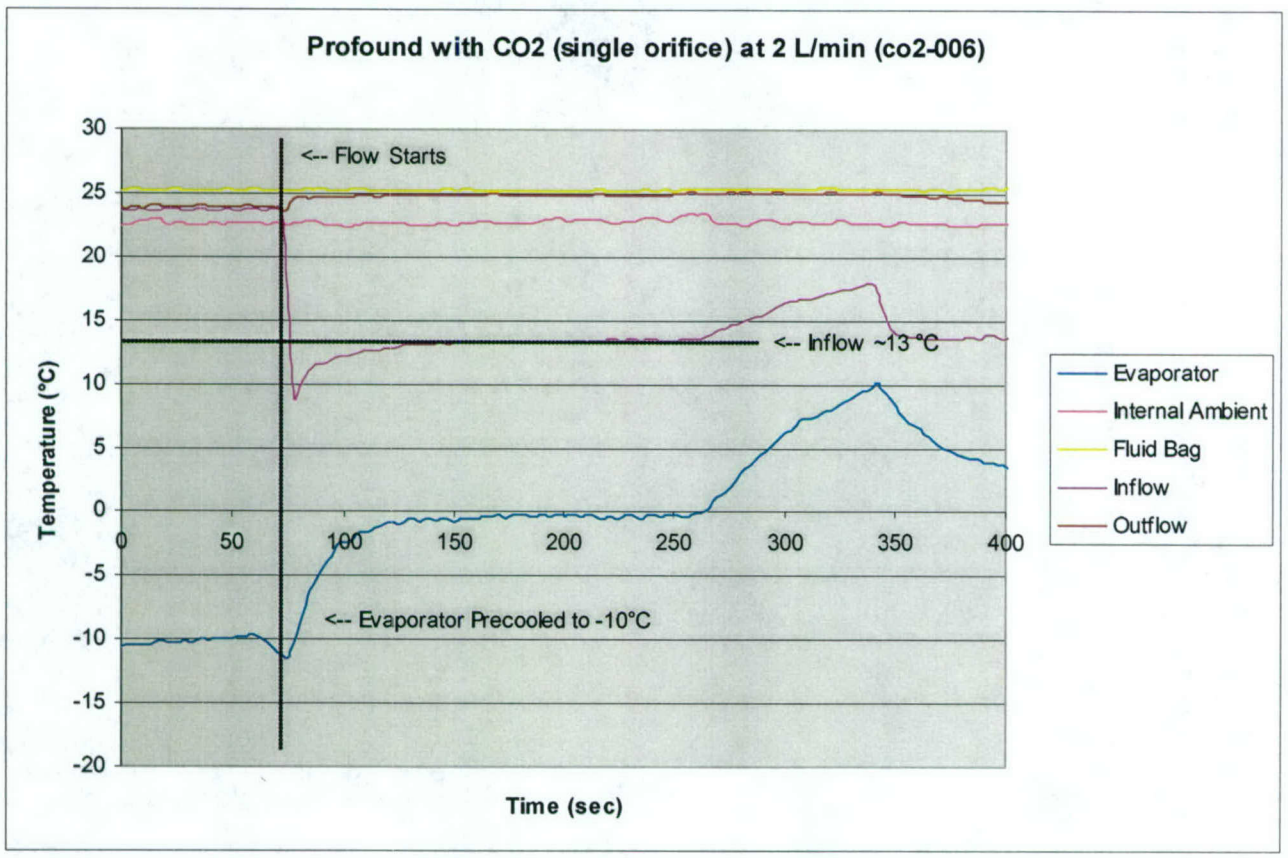


Figure 5 – Temperature Results for Profound Hypothermia – Single Orifice @ 2 L/min

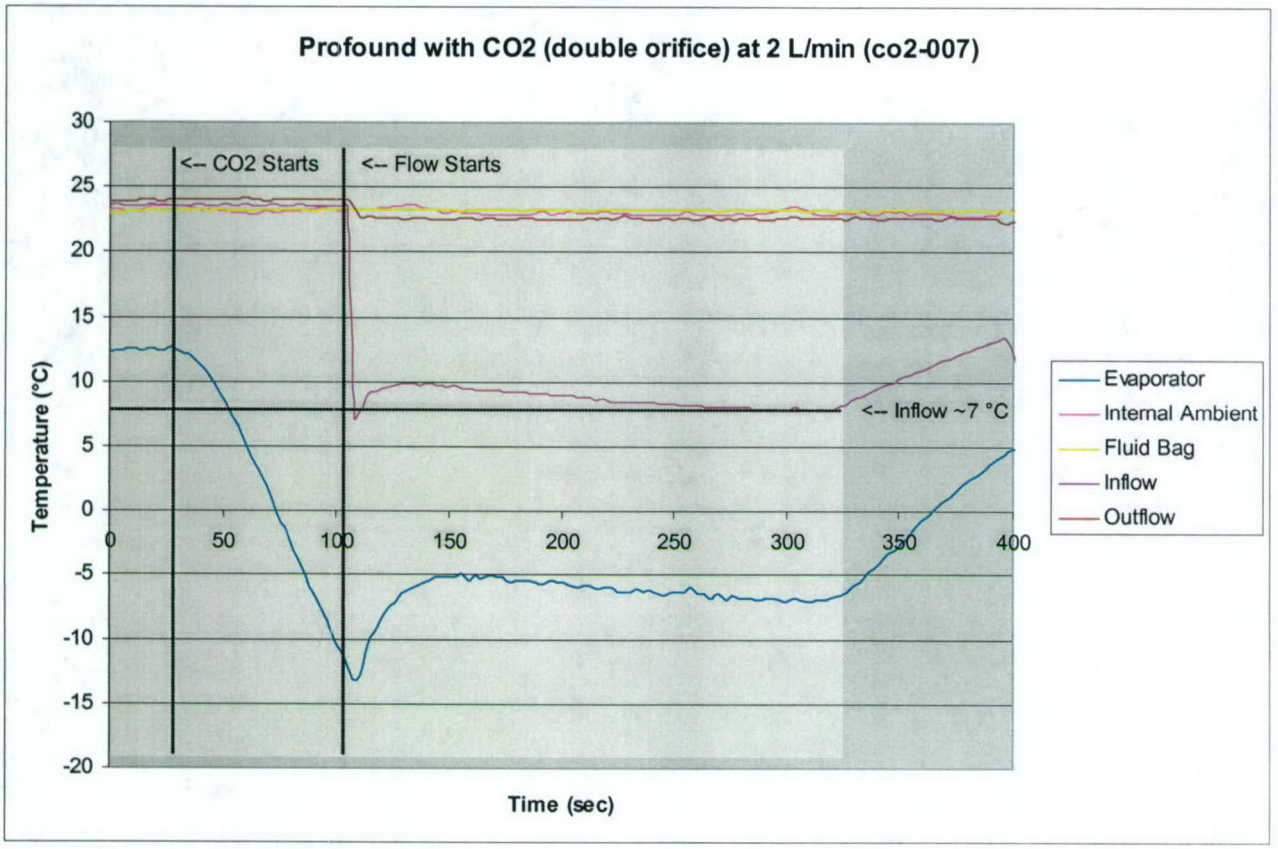


Figure 6 – Temperature Results for Profound Hypothermia – Double Orifice @ 2 L/min

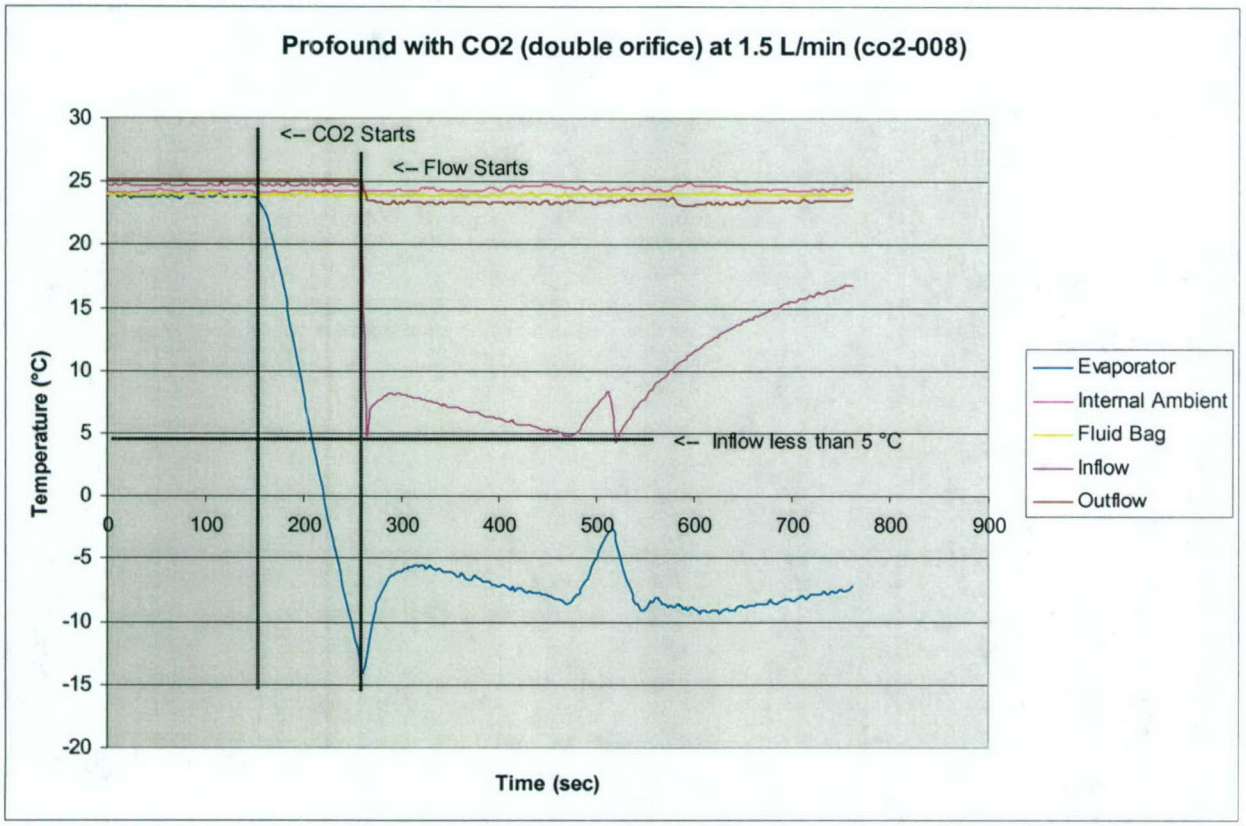


Figure 7 – Temperature Results for Profound Hypothermia – Double Orifice @ 1.5 L/min

Conclusions

Liquid CO_2 cooling compared exceptionally well to mechanical vapor-compression cooling in every aspect to meet criteria for both Mild-Moderate and Profound hypothermia states. Cool down rates, in some instances, where even faster than vapor-compression cooling. Evaporator temperature, in all cases, was cooler than vapor-compression. The only deficiency was not being able to attain the 6-10 °C inflow temperature in the Profound single orifice @ 2 L/min case. However, this would be easily attainable simply by increasing the CO_2 mass flow rate, which was easy to implement with the only drawback of increased CO_2 consumption.

Suggestions for Further Work

The solid dry ice particles entrained in the CO_2 orifice discharge jet had caused minor clogging of the serpentine copper tubing comprising the primary side of the heat exchanger. If an obstruction develops, besides halting blood cooling, full CO_2 container pressure will be present everywhere upstream of the clog. It is therefore imperative that all upstream flow components be designed for at least 1000 psi. The weakest component in the CO_2 flow routing is the soldered external 180° loops in the evaporator (heat exchanger), which are rated at only about 500 psi. However, the few transient clogs that did develop during testing were probably in the first internal 180° loop, since this is one of the coldest locations and research has shown that solid and liquid particulates, when entrained in a gas flow and entering a bend, will separate out and accumulate in the outer, larger radius of the bend due to their greater inertia.

Eliminating clogging is a simple matter of adding a small amount of heat to the flow if the back pressure can not be increased above the CO_2 Triple Point of 75 psia. This can easily be accomplished via natural or forced convection from the environment. All plumbing downstream of the discharge orifice(s), including the heat exchanger, should have good surface exposure via metal to ambient air and no insulation whatsoever. Even stainless steel plumbing should be avoided (due to its lower thermal conductivity compared to copper, aluminum, brass and even carbon steel) unless extra strength is needed for possible clogging situations. If clogging still persists in the heat exchanger (the thickest CO_2 flow component), especially at higher CO_2 flow rates, circulating ambient or heated air via a small fan about the heat exchanger should solve the problem.

Variable flow orifice or multiple orifices, each with an on/off valve would give extra cooling power during a procedure.

Appendix J

ARDIEM

TECHNICAL REPORT

RECORD NO.
AM-00027

TITLE OF TECHNICAL REPORT		REVISION
Concept and Feasibility of a Mild-Moderate Induction Device for Emergency Vehicles		00
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-02	9/3/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Development of a portable unit for EV use	Mike Pitsakis	
TECHNICAL AREA		
SUBJECT AND KEY TECHNICAL WORDS		

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

Abstract

The emergency vehicle hypothermia induction unit must be compactly packaged and ergonomically designed for use inside and outside of emergency vehicles. It must be as lightweight as possible to permit transport and as small as possible to occupy as little space as possible. I estimated the device current draw requirement first based on measured individual component draw and determined the battery specifications and weight. Then I estimated the total weight and size of the unit from existing part weights/sizes. It turns out that the best, under current technology is a unit that utilizes compressed CO2 cooling, weighs about 70 lbs, measuring 2.5ft x 3ft x 1ft or less, and will be good for $1^{1}/_{2}$ hour of pump operation when the battery is fully charged.

Background

The critical requirements associated with designing a portable mild-moderate hypothermia induction device are weight, size, and power for battery operation. The technical reports listed below provide information regarding CO2 cooling feasibility, weight, and power measurements that form the basis of this report.

References

1. Technical report titled "", TR_Hypo 040910 DS.doc, provides information on CO cooling.
2. Technical report titled "Current Draw of Hypothermia Induction Devices and Effect on Portability", TR_Hypo 040622.doc.
3. Technical report "Energy Storage Devices for Possible Use in Portable Hypothermia Device", TR_hypo 030709 MP.doc, provides information regarding energy storage devices applicable for use in a portable hypothermia device.

Introduction

Compressed CO2 makes a portable mild-moderate hypothermia induction device feasible (see Reference 1). Using this cooling method only requires a heat exchanger. It does, however, require a 20 lb cylinder of compressed CO2, which weighs 47 lbs. Note that CO2 is not toxic, however, it is an oxygen reducer; therefore it can only be used outdoors.

The unit must be compactly packaged and ergonomically designed for use inside and outside of emergency vehicles (ambulances, helicopters, military vehicles, etc.). It must be as lightweight as possible to permit transport and as small as possible to occupy as little space as possible. I envision the unit to:

- stand on casters
- have two heavy duty handles on each side on the top
- have easy panel hook up for CO2
- have means for quick replacement of the battery
- be easily maneuvered by one individual unless lifting is necessary for loading, unloading, or going up/down stairs

I estimated the device current draw requirement first based on measured individual component draw and then determined the battery specifications and weight. Then I estimated the total weight and size of the unit from existing part weights/sizes and added estimates of additional parts.

Purpose

The work in this report offers a concept of a portable EV mild-moderate hypothermia induction unit and a feasibility study on the practicality of the concept.

Description of Apparatus and Setup

N/A

Summary of Data and Results

Considering information provided in Reference 2 above, I developed the table shown in Figure 1 and determined the total current draw required to be 2.3 A in worst case when the CO2 valve is on 100% of the time. Using information provided in Reference 3, I recommend a Panasonic battery model LC-RD1217P (rechargeable, sealed lead acid, 14.3 lbs, 7"X3"X6.6") that provides 17 Ah (20h rate).

Component	Current Drawn from 12V Battery (A)
Fan	0.80
Electronics	0.50
Pump at 2 L/min	1.40
CO2 Valve	1.00
Total	2.30

FIGURE 1

Considering the weight of the battery and estimated weights of other components plus frame and panels, I formed the table shown in Figure 2. The predicted total weight will be 66.3 lbs, for aluminum frame and panels. However if plastics are used for the panels, cooling chamber, and parts of the frame, the total weight may be reduced by about 10 lbs.

Component	Weight (lbs)
Battery	14.3
Electronics/controls	1.00
Pump/Motor	8.00
Evaporator	24.00
Frame	15.00
Panels	4.00
Total	66.30

FIGURE 2

The sizes of the major individual units are shown in the table of Figure 3. These could be packaged in a unit of size 2 ft x 2 ft x 1ft.

Component	Size (HxWxD)
Battery	7" x 3" x 6.6"
Electronics	6" x 8" x 1"
Pump Motor	8.8" x 3" x 4.5"
Evaporator w/ CO@ Valve	6" x 10" x 19"

FIGURE 3

Conclusions

A portable mild-moderate hypothermia induction device as described will weigh less than 70 lbs, will be packaged in an enclosure that is 2 ft x 2 ft x 1ft or less, and will be good for $1^1/_2$ hour of pump operation when the battery is fully charged. This is sufficient time to induce mild or moderate hypothermia to a large 120 kg individual.

Suggestions for Further Work

No further work is necessary.

Appendix K

ARDIEM

TECHNICAL REPORT

RECORD NO.
AM-00011

TITLE OF TECHNICAL REPORT		REVISION
Skin Temperature Probe Suitability for use in Profound Hypothermia Induction Device		0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2003-01	04/20/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Temperature Control testing	Mike Pitsakis	

TECHNICAL AREA
Test, Measurement

SUBJECT AND KEY TECHNICAL WORDS
Hypothermia, Feedback Control

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☒ Other

ASSOCIATED REPORTS
TR_Hypo 031223 MP .doc

Abstract

During temperature control testing of the first Profound Hypothermia Induction device prototype, I came across the problem of using a suitable probe for measuring fluid bag temperature. I found that a skin probe is available and decided to evaluate it for possible use with the device. I determined experimentally that the skin probe temperature sensor is the most suitable and accurate for measuring fluid bag temperature.

Background

During temperature control testing of the profound hypothermia induction device described in technical report "Temperature Control Testing of The First Profound Hypothermia Induction Device Prototype" (TR_Hypo 031223 MP .doc), I discovered that I had no suitable temperature probe for measuring the fluid bag temperature. So I used a myocardial probe attached to the bag surface with surgical tape.

Introduction

In searching for a suitable fluid bag probe, I came across a skin probe with YSI400 compatible sensor available from Smith's Level 1. The probe is circular with a 1" self-adhesive area designed for skin temperature measurements. Therefore it appeared that this probe would be ideal for the application.

Purpose

The suitability and accuracy of the Smith's Level 1 YSI 400 compatible skin probe sensor STS-400 is evaluated experimentally.

Description of Apparatus and Setup

Measurement 1
I used a precision thermometer (YSI400A) with a skin probe and a myocardial probe both exposed in air and at close proximity and recorded the ambient temperature.

Measurement 2
I inserted the myocardial probe inside and in the middle of a bag containing pre-chilled tap water through a small hole on the bag surface after shaking to mix the water well. I adhered the skin probe on the bag surface at close proximity to the myocardial probe. Then I recorded the temperatures after 5 minutes of stabilization.

Summary of Data and Results

Measurement 1
Temperature readings:
Skin Probe = 20.44 °C
Myocardial Probe = 20.53 °C.

Measurement 2
Temperature readings:
Skin Probe = 2.05 °C
Myocardial Probe = 20.31 °C.

Therefore even though the sensors are packaged differently in each probe, they measure within +/-0.05 °C. The difference in temperature between bag surfaces and inside is within 2°C which is the smallest gradient observed among all other alternate probe types and placements as described in TR_Hypo 031223 MP.doc.

Conclusions

The skin temperature probe is the most suitable and accurate for measuring fluid bag temperature.

Suggestions for Further Work

No further work is necessary.

Appendix L

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00009

TITLE OF TECHNICAL REPORT		REVISION
Temperature Control Testing of The First Profound Hypothermia Induction Device Prototype		0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2003-01	12/23/03
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT		NAME OF AUTHOR
Temperature Control testing		Mike Pitsakis

TECHNICAL AREA

Test, Measurement

SUBJECT AND KEY TECHNICAL WORDS

Hypothermia, Feedback Control

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☒ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

Abstract

The Profound Hypothermia Induction device prototype, while in operation, has the capability of outputting temperature data to a computer in real time. Such data plus temperature data acquired by an external device were collected, processed, and plotted in order to determine the heat loss of the cold box and the fluid, the cooling rate of the fluid, and the precision of the temperature control. The heat loss of the cold box was determined to be 2.5°C/hr while that of the fluid was not observable in the 1.5 hr measurement. This lends to battery operation. The average cooling rate 1.8°C/hr of fluid is too slow. Therefore it is recommended using pre-chilled fluid bags. Temperature control is better than specification (±0.5°C) with accuracy of ±0.3°C from 0 to 60°C but ±0.2°C in the 32 to 42°C. Temperature gradients inside the cold box are within 0.5°C.

Background

Profound hypothermia is intended for use in trauma-induced exsanguination cardiac arrest or cardiac arrest which cannot be reversed by defibrillation. In these cases, which are considered unresuscitable by standard advanced life support procedures, the profound hypothermia (suspended animation), with or without drugs, is intended to preserve the viability of targeted organs until surgical repairs and delayed resuscitation. The induction of profound hypothermia is accomplished by a rapid large volume cold flush via a specially designed, occluding, aortic balloon catheter (developed under a separately funded program) placed in the thoracic aorta. The flush rapidly cools the heart and brain initially, then abdominal organs with the collapse of the catheter occluding balloon. Cooled fluid and diluted blood may or may not be recirculated depending on the scenario.

Introduction

The first prototype of the Profound hypothermia induction device has been constructed and tested. The device uses vapor-compression refrigeration cycle and a custom designed cold box for cooling or maintaining the fluid contained in a standard 10 L hospital bag. It uses a peristaltic pump for circulating the blood. Temperature control is accomplished by electronically cycling the compressor on/off.

Purpose

Precise temperature control and cooling rate are important to this device and are part of the requirements listed in the preliminary Design Requirements Document. Temperature control verification testing was performed and the results are reported here.

Description of Apparatus and Setup

The device was designed to monitor internal ambient (inside the device), heat exchanger (primary), inflow (to the patient), outflow (from the patient), and two patient temperatures and report these at three (3) second intervals to a computer via a serial link using the Hyperlink program. The data in the computer is saved in a text file containing time stamps of when taken. Further the data must be processed by the extract.tcl program to be formatted in columns for importation into a spreadsheet (EXCEL). YSI #44004 (2252 □ @ 25°C, thermistor Mix "B") temperature sensors were used. These have a ±0.2°C from 0°C to 60°C, ±0.1°C from 32°C to 42°C accuracy (Yellow Spring Instruments data sheet). The Steinhart-Hart model calibrated between -15°C to 45°C is used by software to convert resistance readings to temperature. The 0.1% resistor sensor interface circuit, 12-bit A/D, and the conversion routine add another ±0.1°C to the measurement error (according to the model/simulator spread sheet Mod_Therm YSI.xls). In addition K type thermocouples were used with Yokogawa 110 temperature recorder for measurements with the device turned off.

Summary of Data and Results

To determine the heat loss of the box, I placed K type thermocouples in three different locations inside which was chilled to -6°C power was turned off and all temperatures plus ambient (outside) were recorded. The data was plotted and shown in Figure 1. With ambient temperature averaging 22°C, all three monitored temperatures at different locations inside the cold box are very close and rise at a rate of about 2.5°C/hr.

To determine the fluid heat loss inside the cold box, I used the device data utility. The cold box was chilled to 1°C then the refrigerator was turned off and the temperatures were recorded versus time. A plot is shown in Figure 2. For the hour and a half long measurement time, there was no heat loss associated with the bag fluid.

To determine the cooling rate of the fluid, I placed 10 L bag filled with water in the cold box and let the refrigerator free run. The data plot is shown in Figure 3. The cooling rate is about 1.8°C/hr. the temperature inside the bag was monitored by a myocardial probe placed inside the bag through a hole in the bag wall.

Figure 4 shows evaporator temperature and two bag temperatures. The temperature monitored by the probe that was taped on the bag was used for feedback control. The set point was chosen 5°C. The fluid was chilled to 5°C after some time and was maintained there until some disturbance caused it to drop by 1°C. The difference in temperature between bag surfaces and inside varies from 0 °C to 2°C. This is the smallest gradient observed among all other alternate sensor placements.

Figure 4 shows evaporator temperature and two bag temperatures. The temperature monitored by the probe that was taped on the bag was used for feedback control. The set point was chosen 5°C. The fluid was chilled to 5°C after some time and was maintained there until some disturbance caused it to drop by 1°C. The difference in temperature between bag surfaces and inside varies from 0°c to 2°C. This is the smallest gradient observed among all other alternate sensor placements.

Figure 5 shows plotted data taken during a cold flush experiment using the Pig Simulator with a 10 L fluid bag chilled to 4°C and delivered at 1 L/min. The "patient" cooling rate is about 0.8°C/min.

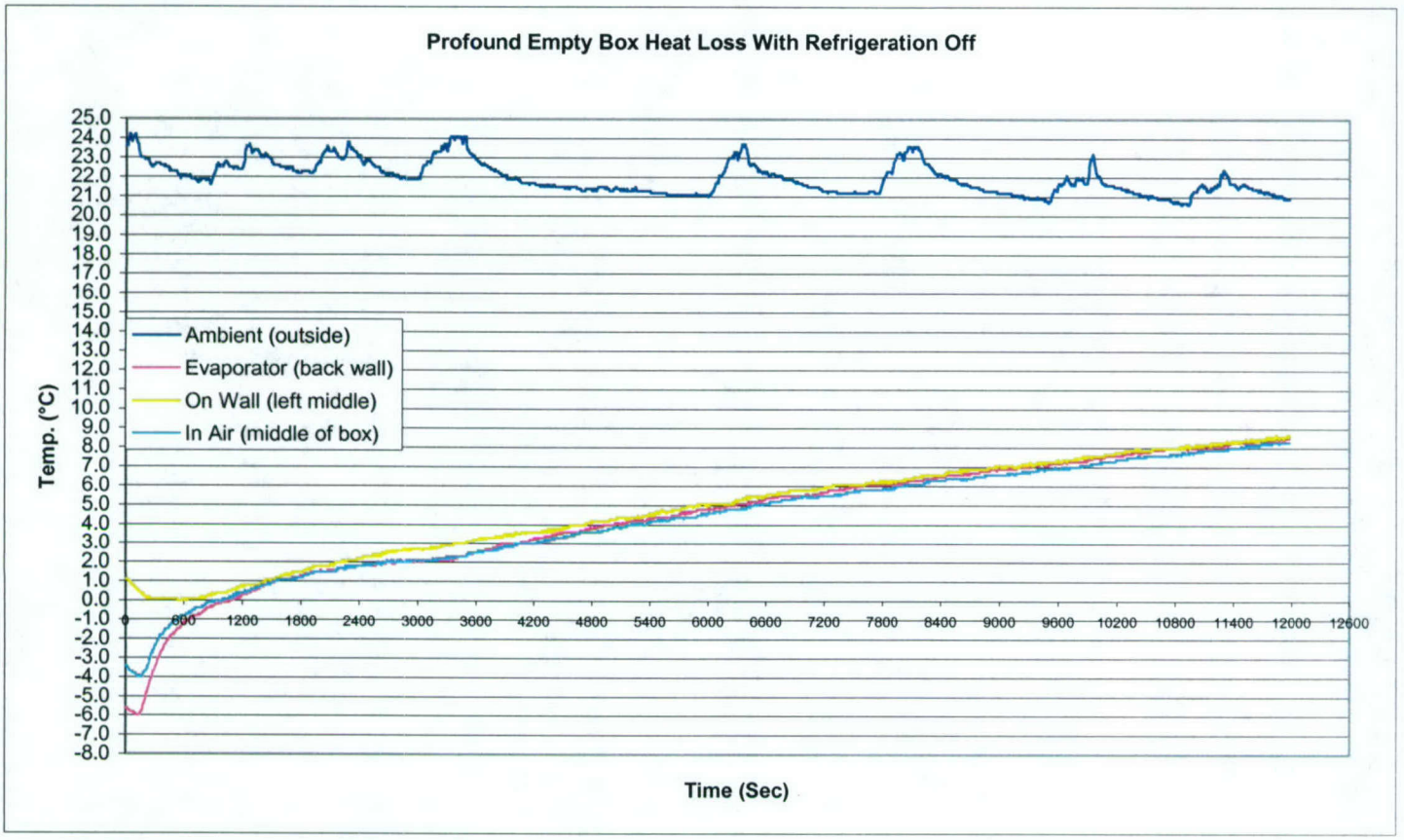


FIGURE 1

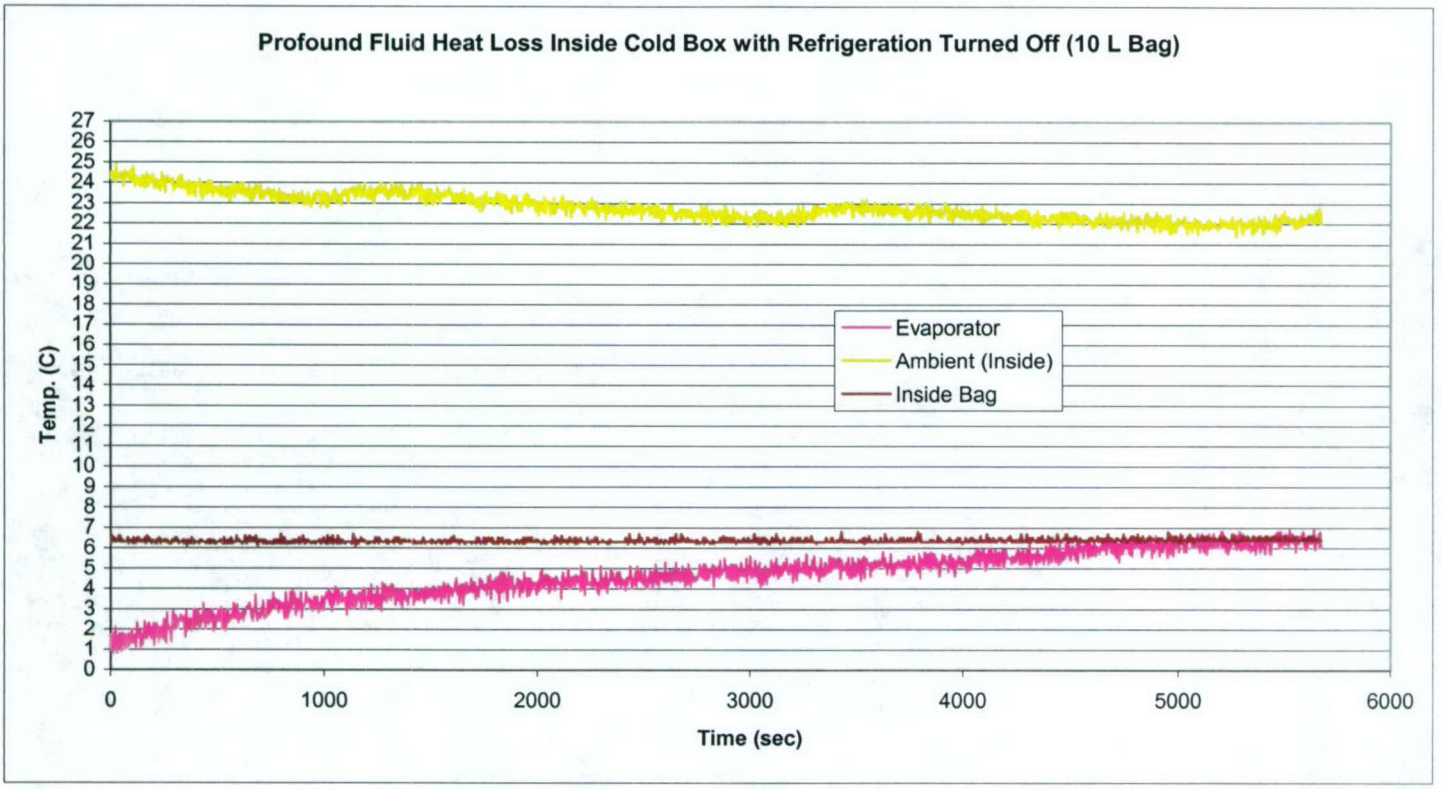


FIGURE 2

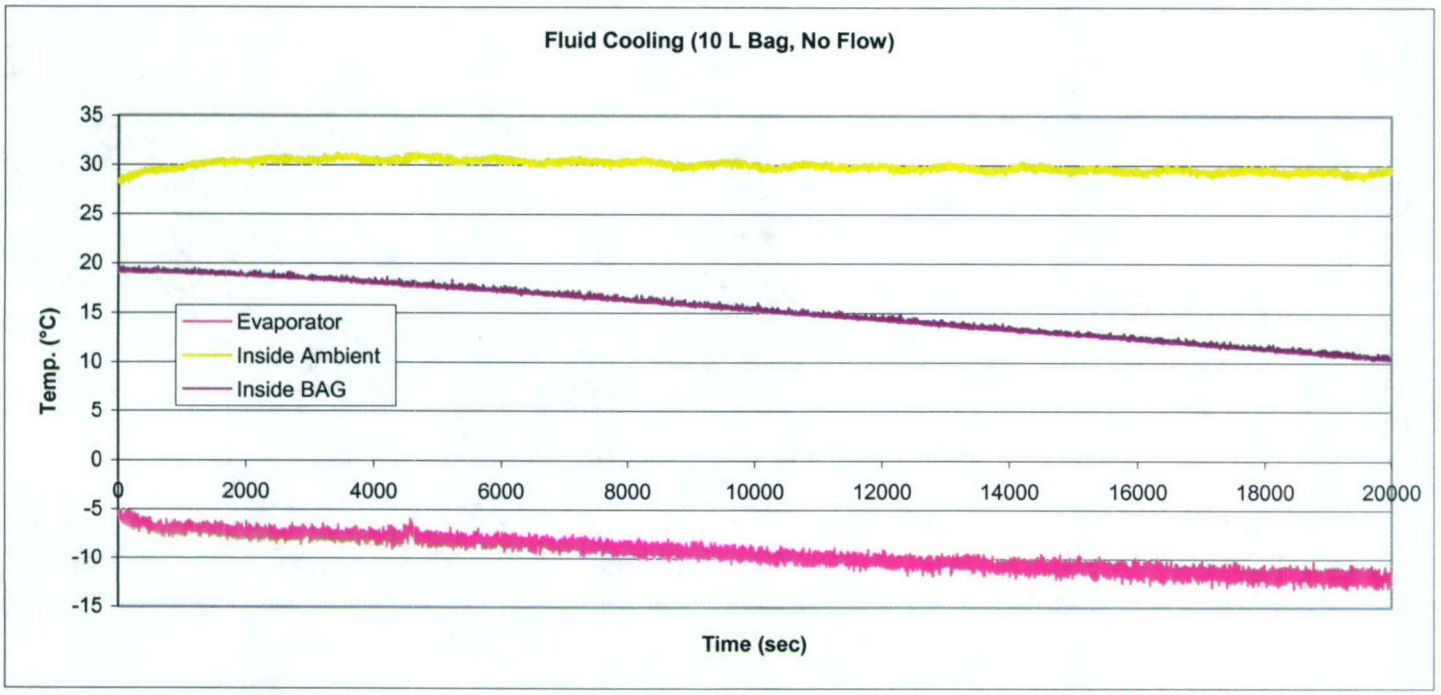


FIGURE 3

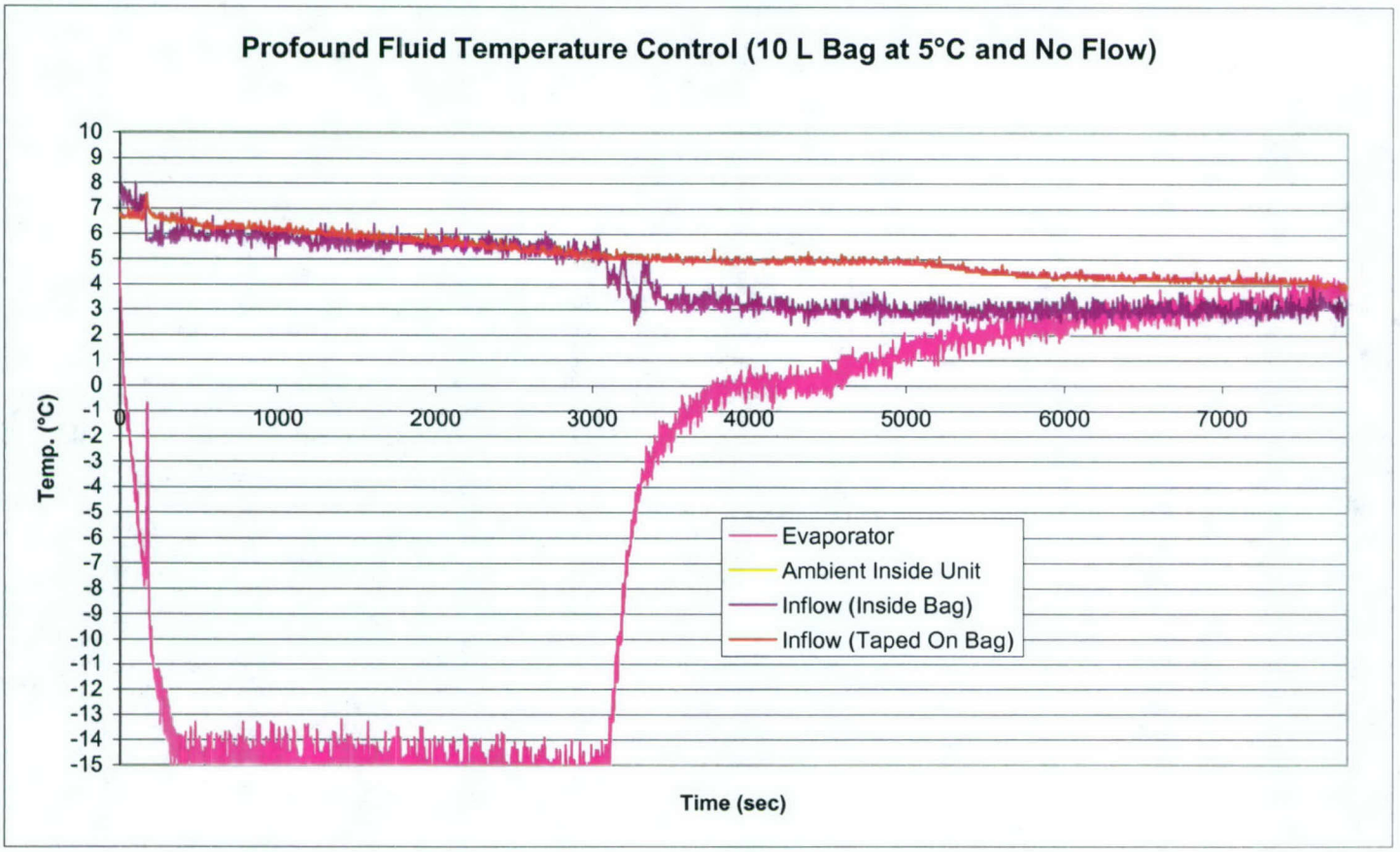


FIGURE 4

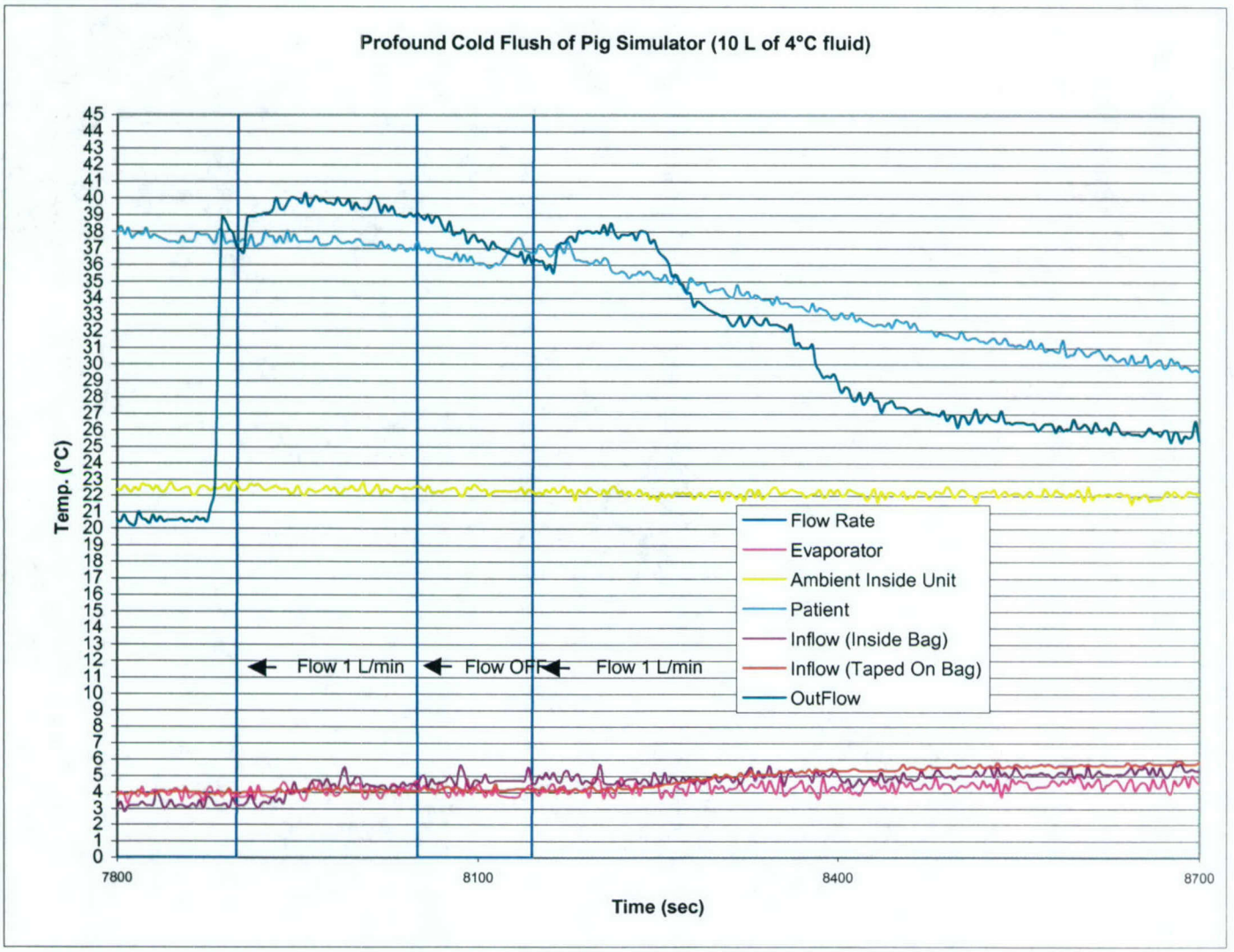


FIGURE 5

Conclusions

The 2.5°C/hr heat loss of the box and no loss of the fluid is good enough to allow turning temperature control off during flush to conserve power in a battery operated unit. The temperatures inside the box are quite uniform (less than 0.5°C spread). The fluid cooling rate is rather slow 1.8°C/hr. It will take more than 10 hours to chill a bag of 10 L fluid from 25°C to 5°C. Therefore it is recommended using pre-chilled fluid bags. Temperature control is better than specification (±0.5°C) with accuracy of ±0.3°C from 0 to 60°C but ±0.2°C in the 32 to 42°C with the exception of the observed disturbance. Taping a sensor on the bag wall or using a skin probe was determined to be the best way for monitoring fluid temperature without puncturing the bag.

Suggestions for Further Work

Temperature tests must be repeated in subsequent prototypes to verify compliance with specification requirements and with data collected by the SCRR in animal experiments.

Appendix M

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00021

TITLE OF TECHNICAL REPORT		REVISION
Temperature Control Testing of the Second Profound Hypothermia Induction Device Prototype		0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-02	06/30/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Temperature Control Testing	Christina Park	

TECHNICAL AREA

Test, Measurement

SUBJECT AND KEY TECHNICAL WORDS

Hypothermia, Feedback Control

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☒ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

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Abstract

The second engineering prototype of the Profound Hypothermia Induction Device (EP2) has been completed and tested for the accuracy of its temperature control. The tests were run and the temperature information was collected via a computer for data processing. This data was then used for calculating the heat loss of the device over time and for graphing purposes. The heat loss of the cold box was found to be very small at only 0.4°C/hr. The fluid heat loss was found to be insignificant at only 0.2°C/hr. The cooling rate for the EXP 2 unit was found to be slightly better than the previous unit with a cooling rate of 5.6°C/hr. It would still take a considerable amount of time to cool the 10L fluid bag; therefore it is still recommended the fluid bags be pre-chilled.

Background

Profound hypothermia is intended for use in trauma-induced exsanguinations cardiac arrest or cardiac arrest, which cannot be reversed by defibrillation. In these cases, which are considered unresuscitable by standard advanced life support procedures, the profound hypothermia (suspended animation), with or without drugs, is intended to preserve the viability of targeted organs until surgical repairs and delayed resuscitation can be performed. The induction of profound hypothermia is accomplished by a rapid large volume cold flush via a specially designed, occluding, aortic balloon catheter (developed under a separately funded program) placed in the thoracic aorta. The flush rapidly cools the heart and brain initially, and then abdominal organs with the collapse of the catheter occluding balloon. Cooled fluid and diluted blood may or may not be recirculated depending on the scenario.

Introduction

The second prototype of the profound hypothermia induction device has been constructed and tested. The device uses vapor-compression refrigeration cycle and a custom designed cold box for cooling or maintaining the fluid contained in a standard 10L hospital bag. It uses a peristaltic pump for circulating the blood. Temperature control is accomplished by electronically cycling the compressor on and off.

Purpose

Precise temperature control and cooling rate are important to this device and are part of the requirements listed in the preliminary Design Requirements Document. Temperature control verification testing was performed and the results are reported here.

Description of Apparatus and Setup

The device was designed to monitor internal ambient (inside the device), evaporator, inflow (to the patient), outflow (from the patient), and two patient temperatures and report these at three second intervals to a computer via a serial link using the Hyperlink program. The data in the computer is saved in a text file containing time stamps of when taken. Further the data must be processed by the extract.tcl program to be formatted in columns for importation into an EXCEL spreadsheet. YSI #44004 temperature sensors were used (2252 @25°C, thermistor Mix "B"). These sensors have an accuracy of ±0.2°C from 0°C to 60°C, and ±0.1°C from 32°C to 42°C (Yellow Spring Instruments data sheet). The Steinhart-Hart model, calibrated between -15°C to 45°C, is used by software to convert resistance readings to temperature. The 0.1% resistor sensor interface circuit, 12 bit A/D, and the conversion routine add another ±0.1°C to the measurement error (according to the model/simulator spread sheet Mod_Therm YSI.xls).

Summary of Data and Results

To determine the heat loss of the cold box when empty, three temperature probes were placed inside the cold box. Patient Temp 1 was placed at the bottom of the box, Patient Temp 2 was placed in the middle of the box, Inflow was placed at the top of the box, and Outflow recorded the ambient temperature. The cold box was chilled to 0°C. Once the set point temperature was met, the temperature control was turned off and the temperatures were recorded as shown in Figure 1. With an average ambient temperature of 26.6°C, the rise in temperature was very small, with only 0.4°C/hr.

To determine the fluid heat loss inside the cold box, the fluid bag and cold box were chilled to 1°C. Once the set point temperature was reached, the temperature control was turned off and the temperatures were recorded over time and plotted in Figure 2. Patient 1 was placed on the middle of the fluid bag. Patient 2 was placed in the middle of the unit. Inflow was placed at the bottom of the unit and Outflow again recorded the ambient temperature. The temperature rise was very small at only 0.2°C/hr.

To determine the cooling rate of the fluid, a 10L bag at ambient temperature was placed into the cold box (also at ambient temperature) and the device was free-run. The Patient 1 temperature probe was placed on the center of the fluid bag and measured the temperature. The temperatures were recorded over a period of time and plotted in Figure 3. The device was found to have an average cooling rate of 5.6°C/hr.

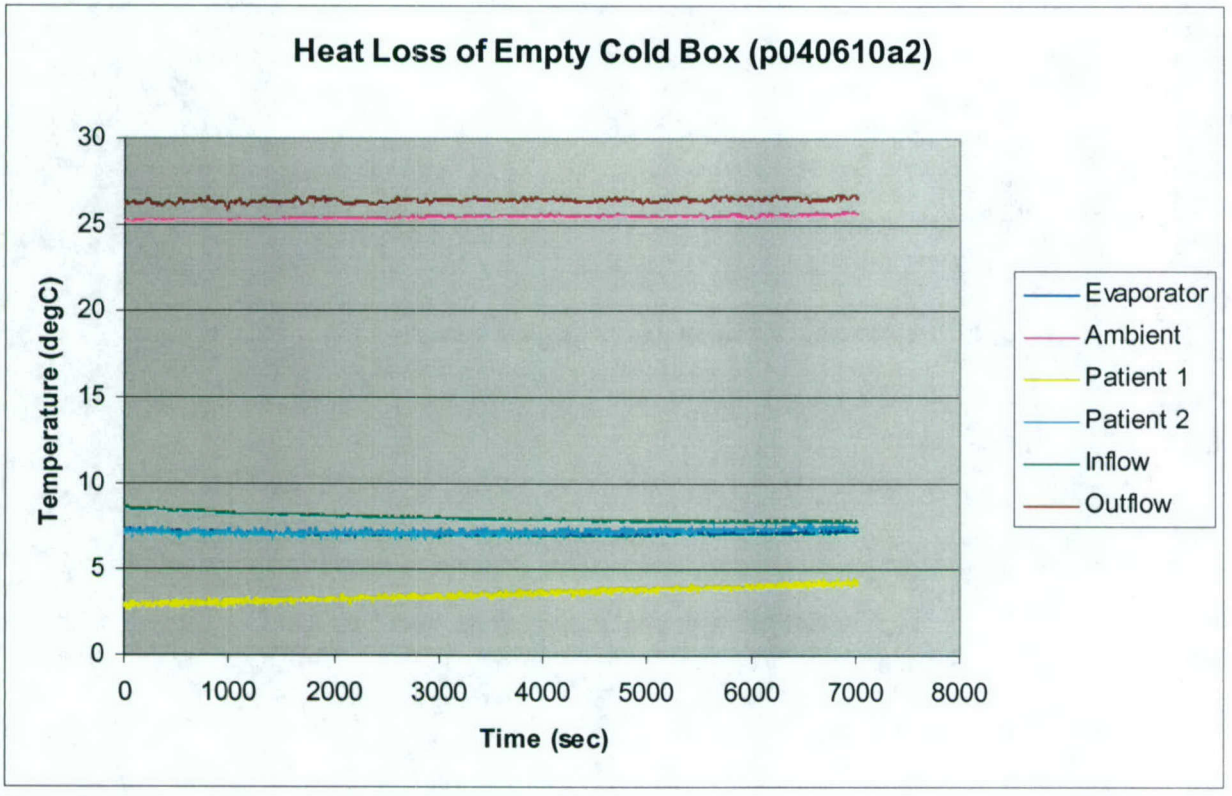


Figure 1

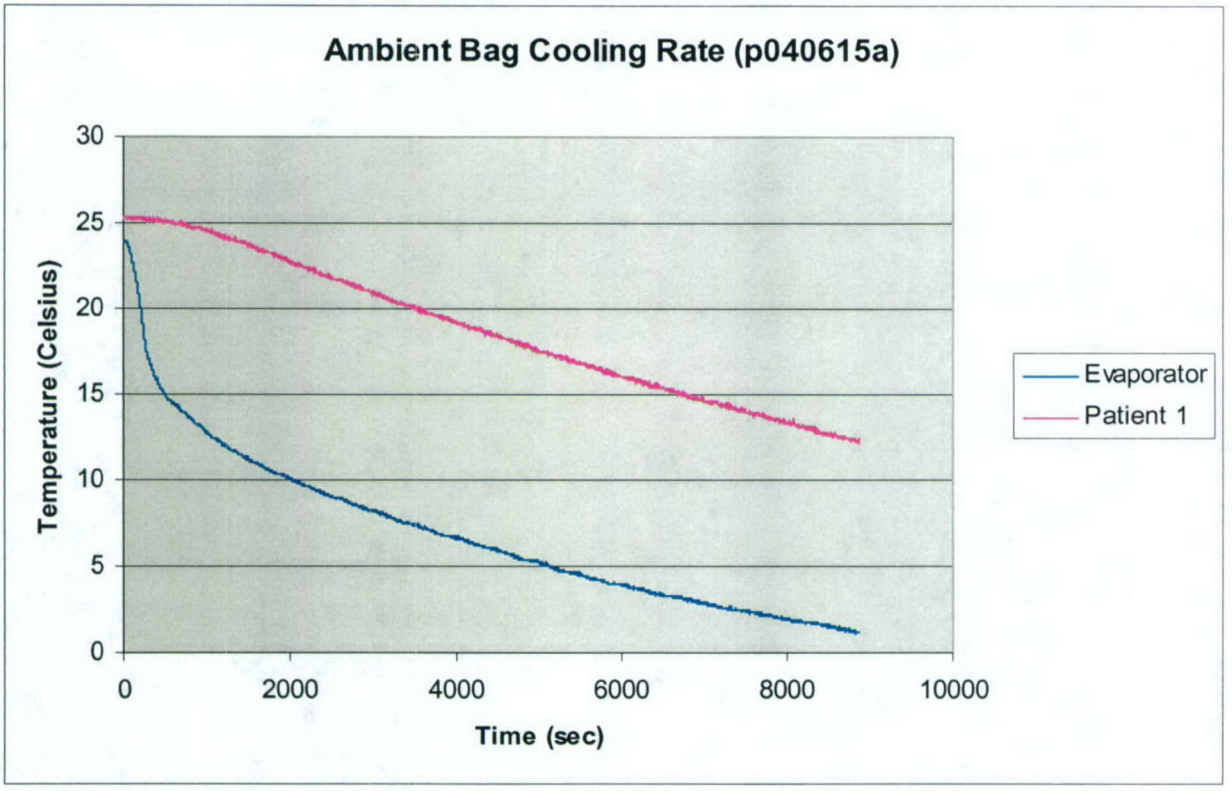


Figure 2

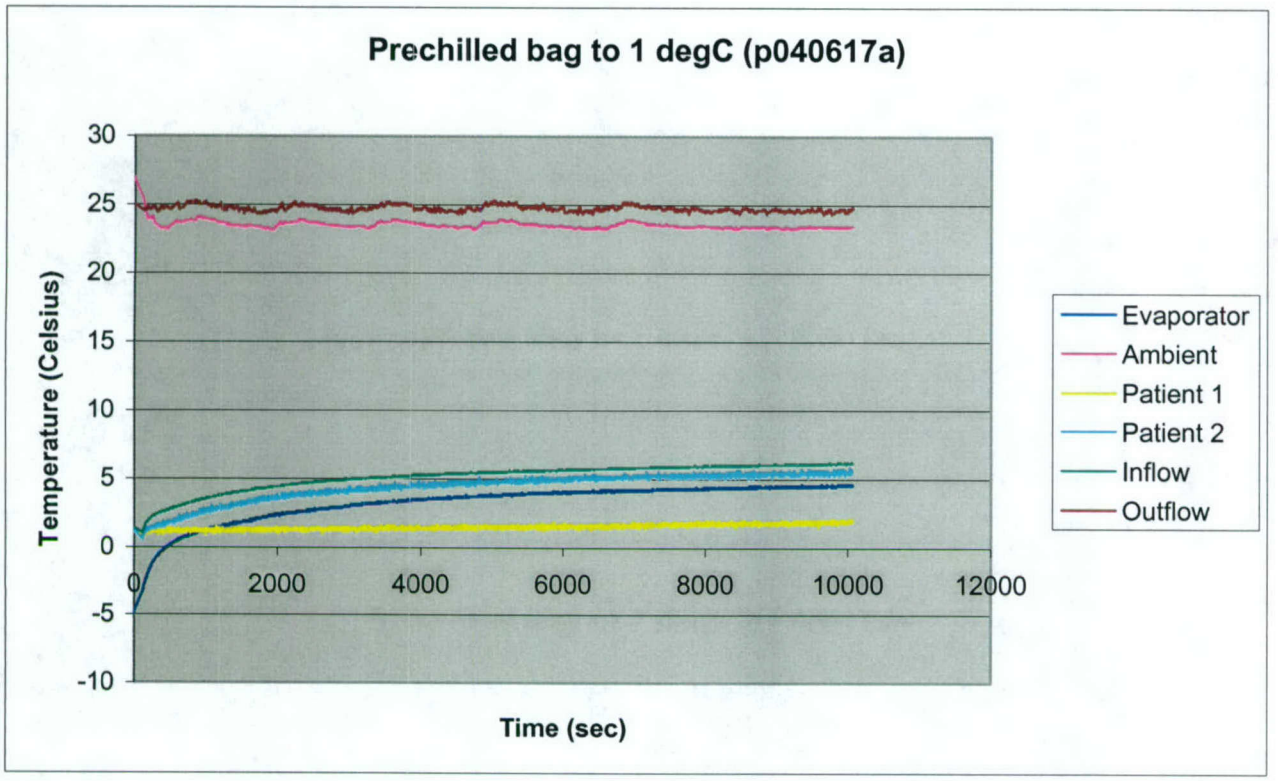


Figure 3

Conclusions

With a maximum heat loss rate of only 0.4°C, it is safe to assume that this unit, EXP2 has an insulating value good enough to allow turning temperature control off during flush to conserve power in a battery operated unit. Although the cooling rate with this unit is better than EXP1 with a rate of 5.6°C/hr, this is still a relatively slow process, and it is still recommended that a pre-chilled bag be used.

Suggestions for Further Work

Temperature tests must be repeated in subsequent prototypes to verify compliance with specification requirements and with data collected by the SCRR in animal experiments.

Appendix N

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00025

TITLE OF TECHNICAL REPORT			REVISION
Temperature Control Testing of the Refined Profound Hypothermia Induction Device Prototype			0
PROJECT OR PROGRAM NAME		PROGRAM NUMBER	DATE
Hypothermia		2004-02	08/26/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT			NAME OF AUTHOR
Fluid Heat Loss			Christina Park
TECHNICAL AREA			
Test, Measurement			
SUBJECT AND KEY TECHNICAL WORDS			
Hypothermia, Heat Loss			
DOCUMENTATION TYPE			
☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☒ Verification	☐ Product Support	☐ Risk Analysis	☐ Other
ASSOCIATED REPORTS			

Abstract

The refined engineering prototype of the Profound Hypothermia Induction Device (EP2) has been completed and needed to have its insulating qualities tested. The test was run and the temperature information was collected via a computer for data processing. This data was then used for calculating the heat loss of the device over time, and for graphing purposes. The heat loss of the pre-chilled fluid bag inside the cold box was found to be 1.02°C/hr.

Background

Profound hypothermia is intended for use in trauma-induced exsanguinations cardiac arrest or cardiac arrest, which cannot be reversed by defibrillation. In these cases, which are considered unresuscitable by standard advanced life support procedures, the profound hypothermia (suspended animation), with or without drugs, is intended to preserve the viability of targeted organs until surgical repairs and delayed resuscitation can be performed. The induction of profound hypothermia is accomplished by a rapid large volume cold flush via a specially designed, occluding, aortic balloon catheter (developed under a separately funded program) placed in the thoracic aorta. The flush rapidly cools the heart and brain initially, and then abdominal organs with the collapse of the catheter occluding balloon. Cooled fluid and diluted blood may or may not be recirculated depending on the scenario.

Introduction

The third prototype of the profound hypothermia induction device has been constructed. The device uses a vapor-compression refrigeration cycle and a custom designed cold box for cooling or maintaining the fluid contained in a standard 20L hospital bag. It uses a peristaltic pump for circulating the blood. Temperature control is accomplished by electronically cycling the compressor on and off.

Purpose

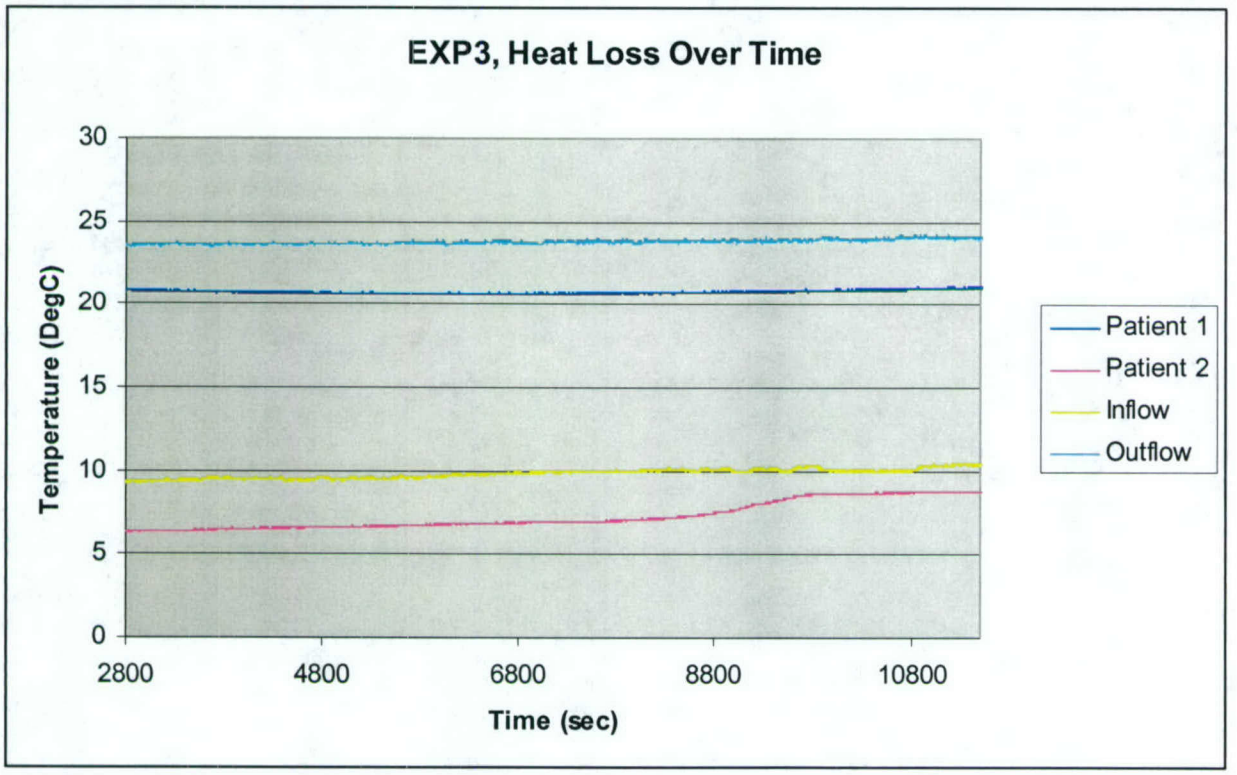
The insulating quality of the new EXP3 Profound Hypothermia device needed to be tested. When using a pre-chilled fluid bag, it is important that the device is insulated well enough to maintain the temperature of the fluid bag, with or without power, for a reasonable amount of time until the procedure is performed.

Description of Apparatus and Setup

The device was designed to monitor internal ambient (inside the device), evaporator, inflow (to the patient), outflow (from the patient), and two patient temperatures, and report these at three-second intervals to a computer via a serial link using the Hyperlink program. The data in the computer is saved in a text file containing time stamps of when taken. Further, the data must be processed by the extract.tcl program to be formatted in columns for importation into an EXCEL spreadsheet. YSI #44004 temperature sensors were used (2252 @25°C, thermistor Mix "B"). These sensors have an accuracy of ±0.2°C from 0°C to 60°C, and ±0.1°C from 32°C to 42°C (Yellow Spring Instruments data sheet). The Steinhart-Hart model, calibrated between -15°C to 45°C, is used by software to convert resistance readings to temperature. The 0.1% resistor sensor interface circuit, 12 bit A/D, and the conversion routine add another ±0.1°C to the measurement error (according to the model/simulator spread sheet Mod_Therm YSI.xls).

Summary of Data and Results

To determine the fluid heat loss inside the cold box, the 20L fluid bag was pre-chilled to 6.3°C. Temperatures were recorded over time and plotted in Figure 1. The Patient 1 temperature sensor was placed at the top of the cold box unit. Patient 2 was placed on the center of the fluid bag. The Inflow temperature sensor was placed at the bottom of the cold box, and the Outflow temperature sensor measured ambient temperature. The temperature rise of the fluid bag was recorded as 1.02°C/hr.



Conclusions

Although the heat loss rate of 1.02°C/hr is slightly higher than previous units, this is to be expected with the changes to the design, such as a plexi-glass door. The heat loss is found to be insignificant and is easily controlled by the condensing unit of the profound device.

Suggestions for Further Work

Temperature tests must be repeated in subsequent prototypes to verify compliance with specification requirements and with data collected by the SCRR in animal experiments.

Appendix O

ARDIEM

DESIGN REQUIREMENTS DOCUMENT

Profound Hypothermia Induction Device for Hospital Use

Program No. 2004-02

Revision 04, Effective 04-20-04

Contents

1. Product Functional Requirements

1.1 Maintainability Requirements

1.1.1 Operator Maintenance

1. Operator maintenance will only be cleaning the surfaces of the device.
2. Describe cleaning in the operator's manual.

1.1.2 Customer Support Maintenance

1. There are no customer support maintenance requirements.

1.1.3 Verification and Validation

1. Perform verification of Maintainability Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Maintainability Requirements on a Manufacturing Prototype.

1.2 Operational Requirements

1.2.1 Intended Use

1. The device is to be used for the induction of profound hypothermia (core body temperature between 10°C to 20°C). Profound hypothermia is induced by initiating a rapid one-way flush with a large volume (10 or more liters) of cold solution via a specialized catheter.
2. The device will be applicable to 95% of children, adolescent, and adult population as defined in the AAMI / ANSI HE74-2001 Human factors design process for medical devices.

1.2.2 Physical Description

1. The device will be housed in a framed enclosure and consist of an inner cooling chamber capable of holding four filled 10-liter fluid bags or fluid containers of sterile solution, a refrigeration system, a pumping system, custom electronics, inputs and readout for patient temperature sensors, flow sensor, pressure sensor, bubble detector, tubing occluder, and a disposable infusion set.
2. The disposable infusion set will consist of fluid bag or container, 1 m long L/S-18 tubing, a bubble trap/filter, and a flow sensor.
3. The device will be movable with wheels for ease of movement such that a single individual can maneuver it.
4. The device weight will be a maximum of 50 kg when loaded with fluid.
5. The device dimensions will be a maximum of 100 cm X 75 cm X 50cm (H X W X D).

1.2.3 Operating Modes

1.2.3.1 Fluid Cooling Mode

1. This is an optional mode for cooling the fluid if pre-chilled fluid is not used. It will take 5 to 10 hours for this depending on initial fluid temperature and fluid volume.
2. The operator will insert up to four fluid bags in the cooling chamber and attach a skin temperature probe on one of the bags.
3. The device will attempt to chill the fluid to $1^{\circ}C \pm 0.5^{\circ}C$ then automatically enter Standby Mode.
4. The device on power on will always start in Fluid Cooling Mode and will return to this mode when it detects warm fluid.

1.2.3.2 Standby Mode

1. The device will attempt to maintain the cooling chamber at 0°C ± 0.5°C in order to keep the fluid ready for operation.
2. The device will turn indicator light READY on to alert the operator that it fluid is ready for a procedure if the fluid temperature is equal or less than 2°C.

1.2.3.3 Flush Mode

1. In this mode the device will deliver the fluid through the disposable tubing-set and catheter to the patient at a rate between 0.5 and 2 L/min ±10% as selected by the operator. Note that the catheter (3mm bore x 1.5 meter long) is not a part of the device.
2. The operator will install and prime the tubing set by selecting PRIME flow rate.
3. The operator will select a flow rate and depress a green switch to start the pump and cold flush.
4. The operator will replace empty fluid bags with full fluid bags as needed during the course of the procedure.

1.2.4 Operator Interface

1.2.4.1 The operator input interface will consist of a means of selecting the following parameters:

1. Device power on/off.
2. Fluid flow rate.
3. Fluid flow on/off.
4. A means for connecting the tubing-set pump section and connecting to the fluid bag.

1.2.4.2 The device output to the operator will consist of the following:

1. Device power on/off indicator (RED).
2. Flow rate selection and display.
3. Device READY indicator (GREEN).
4. Device Alert indicator (YELLOW).
5. Patient temperature display.
6. Pressure display.
7. Volume of totalized dispensed fluid.
8. Elapsed time of procedure.

1.2.5 Training

1. Provide sufficient information in educational materials, labeling, and operator's manual.

1.2.6 Verification and Validation

1. Perform verification of Operational Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Operational Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

1.3 Quality Requirements

1.3.1 General

1. The manufacturing processes will assure the device is free from defects and meets all product specifications.
2. The quality system used in the design, manufacture, packaging, labeling, storage, installation, and servicing of the device will comply with the applicable requirements of the following:
   - The FDA Quality System Regulation (FDA QSR) as defined in 21CFR, Parts 820, latest revision
   - ISO 13485:2003(E), Medical Devices – Quality management systems – Requirements for regulatory purposes
   - Any other applicable standard or regulation referenced in the FDA QSR or ISO 13485:2003(E).

1.3.2 Verification and Validation

1. Perform verification of Quality Requirements on both the Engineering and Manufacturing Prototypes.
2. Validate the Quality Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

1.4 Repairability Requirements

1.4.1 General

1. Company authorized service centers or factory service personnel will perform all repairs.
2. Design the device to allow easy internal access to perform repairs.
3. Develop a service manual with sufficient detail for a trained service technician to isolate failures.

1.4.2 Verification and Validation

1. Perform verification of Repairability Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Repairability Requirements on a Manufacturing Prototype.

2. Product Performance Requirements

2.1 Durability Requirements

2.1.1 Shock and Vibration

1. Shipping The device will withstand normal levels of shock and vibration without incurring functional damage when in the shipping configuration in accordance with ISTA Procedure 1B.

2.1.1.2 Handling

1. The device will withstand, in the uncrated configuration, hitting walls and other fixed obstacles at a walking speed and moving in and out of elevators and over thresholds at walking speed.

2.1.1.3 Solvents and Fluids

1. All exposed surfaces will be resistant to damage from commonly used hospital/clinical cleaning fluids (such as alcohol and 10% bleach) and contact with salts, bodily fluids, and glucose solutions.

2.1.1.4 RFI and EMI

1. The device will meet the RFI and EMI immunity requirements listed in 2.2.1 1-4

2.1.1.5 Verification and Validation

1. Perform verification of Durability Requirements on Engineering Prototypes at an external test facility. After each test run, perform a functional test to verify the device performance. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Durability Requirements on a Manufacturing Prototype.

2.2 Environmental Requirements

2.2.1 EMC Requirements

1. Medical Electrical Equipment EMC: EN 60601-1-2: 2001
2. Radiated and Conducted Emissions: EN 55011: 1998 +A1: 1999 +A2: 2002, FCC Part 15
3. Electrostatic Discharge Immunity: EN 61000-4-2: 1995 +A1: 1998 +A2: 2001
4. Radiated Electromagnetic Field Immunity: EN 61000-4-3: 2002 +A1: 2002
5. Electrical Fast Transient / Burst Immunity: EN 61000-4-4: 1995 +A1: 2001 +A2: 2001
6. Surge Immunity: EN 61000-4-5: 1995, +A1: 2001
7. Power Harmonics, EN 61000-3-2: 2000
8. Voltage Fluctuation (Flicker): EN 61000-3-3: 1995, +A1: 2001

2.2.2 Operating Requirements

1. Ambient Temperature: 10°C to 40°C (IEC601-1, Section 10.2.1a)
2. Relative Humidity: 30% to 75% (IEC601-1, Section 10.2.1b)
3. Atmospheric Pressure: 525mm Hg to 795 mm Hg(IEC601-1, Section 10.2.1c)

2.2.3 Storage Requirements

1. Ambient Temperature: -40°C to 70°C (IEC601-1, Section 10.1a)
2. Relative Humidity: 10°% to 100% max non-condensing relative (IEC601-1, Section 10.1b)
3. Atmospheric Pressure: 525mm Hg to 795 mm Hg (IEC601-1, Section 10.1c)

2.2.4 Verification and Validation

1. Perform verification of EMC Environmental Requirements on a Manufacturing Prototype at a certified test facility.
2. Perform verification of Operating and Storage Environmental Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
3. Validate the Operating and Storage Environmental Requirements on a Manufacturing Prototype.

2.3 Performance Requirements

2.3.1 Electrical Requirements

2.3.1.1 Electrical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with UL 26601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety.
2. Use relevant components that are approved by at least one agency.

2.3.1.2 Power

1. Use a power cord that is tested and certified to meet European Community electrical safety requirements for EU approval.
2. Use a power cord that is tested and certified to meet United States electrical safety requirements for FDA approval.
3. Fuse each side of the mains.
4. Line Voltage: 115 VAC +/-10% or 230 VAC +/-10%.
5. Line Power: 200 VA maximum.
6. Line Frequency: 60 Hz +/- 3% or 50 Hz +/-3%.

2.3.1.3 Verification and Validation

1. Perform verification of Electrical Safety Requirements on a Manufacturing Prototype at an external test facility. Perform verification of all other applicable Electrical Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Electrical Requirements on a Manufacturing Prototype.

2.3.2 Electronic Requirements

2.3.2.1 Central Processing Unit

1. Use a central processing unit (CPU) to control the overall operation of the device, including data acquisition, electro-mechanical components, operator interfaces, and communications interfaces.
2. Provide the capability to reset the CPU without cycling power off and on.

2.3.2.2 Real-Time Clock

1. Maintain the device's total operation time over its life.
2. Use a real-time clock (RTC) to associate a specific date and time with each reported measurement.
3. The RTC will continue to operate in the absence of AC line power.

2.3.2.3 PCBAs

1. Design the device with no more than three (3) PCBAs.

2.3.2.4 Operator input

The operator will input the following data:

1. Power on/off will be initiated by a switch
2. The flow rate will be entered via a touch-screen using values between 0.5 and 2 L/min.
3. The pump will shut down immediately if the operator depresses a red emergency switch.

2.3.2.5 Operator output

The following data will be output from the device:

1. A light indicator will indicate that power is on.
2. The fluid temperature will be displayed in °C via a touch-screen with an accuracy of ±0.3°C over the range of –10°C to 40°C.
3. The fluid flow rate will be displayed in mL/min via a touch-screen with an accuracy of 5%.
4. The fluid pressure will be displayed in mmHg via a touch-screen over the range of 0 – 1500 mmHg with an accuracy of +/-10mmHg.
5. The patient temperature will be displayed in °C via a touch-screen with an accuracy of ±0.3°C over the range of -10°C to 40°C.
6. Display totalized volume of dispensed fluid in L via a touch-screen with an accuracy of 5%.
7. Display elapsed time at the start of the pump in minutes.
8. Display warning messages relating to various device and operation faults and conditions via the touch-screen.

2.3.2.6 Device diagnostics

1. The electronics will enable device diagnostics.

2.3.2.7 Safety limits

1. The electronics will detect the existence of bubbles in the extra-corporeal circuit fluid that are greater than 20μL and automatically activate the occluder, shut down the pump, and display a warning message for the condition. The device will then prompt and require user input to either resume operation or enter Cooling Mode.

2.3.2.8 Verification and Validation

1. Perform verification of Electronic Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Electronic Requirements on a Manufacturing Prototype.

2.3.3 Embedded Software

2.3.3.1 General

1. Control overall system operation.
2. Invoke operator input.
3. Provide operator output.
4. Control temperature.
5. Control flow.

2.3.3.2 Data Collection, Processing, and Relaying

1. Acquire temperature, flow, pressure, and other data.
2. Compute flow, temperature, and pressure time averages.

3. Compute elapsed time.
4. Display average fluid and patient temperatures.
5. Display average fluid flow rate and pressure.
6. Display totalized volume of dispensed fluid.
7. Display elapsed time of procedure.
8. Save all data temporarily with time stamps.

2.3.3.3 Test and Diagnostics

1. Perform tests to detect faults.
2. Display fault messages using touch-screen.

2.3.3.4 Safety limits

1. The software will display a device warning message if the fluid temperature drops below –1°C.
2. The software will display a device warning message if the fluid flow rate is outside the tolerance range.
3. The software will display a device warning message if the tympanic patient temperature drops below 9°C.
4. The software will shutdown the pump and display a warning message if the fluid pressure exceeds 800 mmHg when a 3mm catheter is used.
5. The software will shutdown the pump and display a warning message when the total volume of the fluid is dispensed.
6. When either condition 4.) or 5.) above is encountered, the device will prompt and require user input to either resume operation or enter Cooling Mode.

2.3.3.5 Verification and Validation

1. Perform verification of Embedded Software Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Embedded Software Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

2.3.4 Mechanical Requirements

2.3.4.1 General

1. Provide easy access to cooling chamber.
2. Provide easy access to the pump head.
3. Provide easy access to the sensors (pressure and flow) and sensor inputs (temperature).
4. Provide easy access to the operator interface.

2.3.4.2 Thermal Requirements

1. Isolate the electrical/electronics compartment from the refrigeration compartment.
2. Limit the internal device temperature to 40°C under normal operating conditions.
3. Limit the cooling chamber heat-loss to 2°C/hour under normal operating conditions.

2.3.4.3 Mechanical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with the mechanical

safety requirements of UL 60601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety. Also, design and manufacture the device to comply with safety requirements for specific components or systems, such as refrigerating systems (ISO 5149:1993 Mechanical refrigerating systems used for cooling and heating – Safety requirements, and ASHRAE Standard 15-2001 – Safety Standard for Refrigeration Systems), fan guarding (ISO 12499:1999 Industrial fans – Mechanical safety of fans – Guarding), and electromechanical relays (IEC 61810-1:2003 Elementary relays -- Part 1: Safety and general requirements).

2.3.4.4 Verification and Validation

1. Perform verification of Safety Requirements on a Manufacturing Prototype at an external test facility.
2. Perform verification of other Mechanical Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
3. Validate the Mechanical Requirements on a Manufacturing Prototype.

2.4 Reliability Requirements

1. Useful service life willbe five (5) years with normal servicing and maintenance.
2. Design unit with 2000 hours mean MTBF and 24 hours MTTR.
3. Perform verification of Reliability Requirements on Engineering Prototypes by analysis based on MIL STD 217. Also perform FMEA on Engineering Prototypes according to IEC 60812 (1985).

2.5 Safety Risk Management Requirements

2.5.1 Safety Modes

For purposes of evaluating risk and determining the proper performance of failure detection and safety in the design, safe operation is defined as one of the following:

1. The ability to detect fault conditions and alert the operator constitutes the primary safety mode of the system.
2. The ability to detect a threatening condition and alert the operator constitutes the secondary safety mode of the system.
3. The tertiary safety mode will be to shut down the pump.

2.5.2 General Risks

1. Identify undesirable system operating conditions with a system risk analysis. The design will anticipate, to the extent possible, the occurrence of failure modes and provide a means of protecting against them. (EN ISO 14971:2000 Medical devices – Application of risk management to medical devices)
2. General surgical procedural risks, those common to all surgical procedures, are outside the boundaries of the risk assessment for this device.
3. Evaluate risk per EN ISO 14971:2000 Medical devices – Application of risk management to medical devices.
4. Instructions and labeling must fulfill requirements of: FDA Title 21 CFR Part 801 Labeling; MDD 93/42/ EEC, Annex 1, Essential Requirements; EN 1041 Information supplied by the manufacturer with medical devices; EN 980+A1 Graphical symbols for use in the labeling of medical devices; and requirements of Ardiem Medical material handling and quality procedures.
5. Include adequate operator safety instructions in manuals and labeling supplied with the device.

2.5.3 Verification and Validation

1. Perform verification of Safety Risk Management Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Safety Risk Management Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, ISO 14971:2000, and other applicable standards referenced therein.

3. Product Interface Requirements

3.1 Customer Interface Requirements

3.1.1 General

1. Provide appropriate instructional materials (operator's manual, training video, screen prompts, etc.) to allow operator to correctly install and use the device.

3.1.2 Display

1. The device will contain a medium size (12-inch) touch-screen display.
2. The display will be readable under all ambient light conditions.
3. The device will display temperature, error and fault messages to the operator for communicating to a service technician.

3.1.3 Controls

1. All controls via the touch-screen except for power on/off and emergency pump off.

3.1.4 Language

1. Allow factory configuration to a minimum of one language out of future supported languages.
2. Include the following supported languages as a minimum: English (U.S.)
3. Use symbols in accordance with EN 980.

3.1.5 Units of Measure

1. Label controls and display selected and measured values in the following units of measure:
   - Liters (L)
   - Liters per minute (L/min)
   - Degrees centigrade (^{o}C)
   - Millimeters of Mercury (mmHg, cmHg for EU)
   - Minutes (min)

3.1.6 Verification and Validation

1. Perform verification of Customer Interface Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Customer Interface Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

3.2 External Interface Requirements

3.2.1 General

1. The device will contain a serial port capable of communications with a computer to output diagnostics and procedure data .
2. Use a RS-232 with a DB-9 connector as the serial port electrical interface.
3. Use serial port communications at a maximum baud rate of 4800 baud.
4. Use a detachable hospital grade power cord that meets safety requirements.
5. Use a power inlet that meats safety requirements.

3.2.2 Verification and Validation

1. Perform verification of External Interface Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the External Interface Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

3.3 Labeling Requirements

3.3.1 General

1. Manuals and labels will conform to both European Community (93/42/EEC MDD) and FDA (Title 21 CFR 801) requirements.
2. All labels and manuals will comply with requirements of EN 1041, EN 980, and any other applicable standards.
3. Labeling will also contain the following wording prominently displayed: "CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician."

3.3.2 Safety and Warning Labels

1. Provide adequate safety labels per 93/42/EEC MDD, Title 21 CFR 801, EN 1041, EN 980, and ISO 15223.
2. Identify and explain any warnings in the operator's manual.

3.3.3 Shipping Labels

1. TBD

3.3.4 Verification and Validation

1. Perform verification of Labeling Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Labeling Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

3.4 Service Delivery Requirements

3.4.1 General

1. Deliver all necessary information and support products with the main product delivery.
2. Develop a service manual with sufficient detail for a trained service technician to isolate failures.
3. A training program will be available for training of repair and maintenance personnel.
4. Provide training, or training media (CD-Rom, Printed Manual, or through the website) for clinical technicians in the appropriate operation of this product.
5. Ardiem Medical authorized service centers or factory service personnel will perform all repairs.

3.4.2 Verification and Validation

1. Perform verification of Service Delivery Requirements on Engineering Prototypes. Confirm verification on Manufacturing Prototypes if necessary.
2. Validate the Service Delivery Requirements on a Manufacturing Prototype in a clinical trial. Clinical trial results will conform to applicable European Community and Federal Food and Drug Administration Regulations including, but not limited to, the latest revision of EN 540, 21 CFR 812, and applicable standards referenced therein.

4. Revisions

Rev.	Description	Author	Effective Date
00	Preliminary Issue	Ralph Gill	9/26/02
01	Completed Requirements	Mike Pitsakis	9/24/03
02	Updated references to industry regulation and standards	Joseph Klingensmith	10/02/03
03	Revised Functional/Performance, and Interface requirements after input from SCRR and design input review.	Mike Pitsakis	02/20/04
04	Revised some requirements to be consistent with the System Spec Document	Mike Pitsakis	04/16/04

Appendix P

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00020

TITLE OF TECHNICAL REPORT		REVISION
Concept and Feasibility of a Profound Induction Device for Emergency Vehicles		00
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-02	6/28/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT		NAME OF AUTHOR
Development of a portable profound unit for EV use		Mike Pitsakis

TECHNICAL AREA

SUBJECT AND KEY TECHNICAL WORDS

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

Abstract

The emergency vehicle profound hypothermia induction unit must be compactly packaged and ergonomically designed for use inside and outside of emergency vehicles. It must be as lightweight as possible to permit transport and as small as possible to occupy as little space as possible. I estimated the device current draw requirement first based on measured individual component draw and determined the battery specifications and weight. Then I estimated the total weight and size of the unit from existing part weights/sizes. It turns out that the best, under current technology is a unit that weighs about 105 lbs when filled with 20 L of fluid, measuring 2.5ft x 3ft x 1ft or less, and will be good for 6 hours of operation and for 1 hour of pump operation when the battery is fully charged.

Background

The critical requirements associated with designing a portable profound hypothermia induction device are weight, size, and power for battery operation. The technical reports listed below provide information regarding weight and power measurements that form the basis of this report.

References

1. Technical report titled "Profound Hypothermia Induction Prototype Device Weight Analysis", TR_Hypo 030916 RG.doc.
2. Technical report titled "Current Draw of Hypothermia Induction Devices and Effect on Portability", TR_Hypo 040622.doc.
3. Technical report "Energy Storage Devices for Possible Use in Portable Hypothermia Device", TR_hypo 030709 MP.doc, provides information regarding energy storage devices applicable for use in a portable hypothermia device.
4. Technical report titled "Temperature Loss Comparison with several types of insulators", TR_Hypo 040616 CP.doc, provides information on some insulator measurements.

The profound hypothermia induction device engineering prototype was designed using exclusively 12 VDC powered components for easy transition to a portable battery operated unit.

Introduction

The unit must be compactly packaged and ergonomically designed for use inside and outside of emergency vehicles (ambulances, helicopters, military vehicles, etc.). It must be as lightweight as possible to permit transport and as small as possible to occupy as little space as possible. I envision the unit to:

- hold a 20 L fluid bag (~44 lbs). Note that this is the minimum amount of fluid
- stand on coasters
- have two heavy duty handles on each side on the top
- have the cooling chamber access on top with the pump next to it and the controls next to the pump
- have means for quick replacement of the battery
- use lightweight polyurethane, polypropylene, or polyethylene foam for insulation (see Reference 4.)
- be easily maneuvered by one individual unless lifting is necessary for loading, unloading, or going up/down stairs

I estimated the device current draw requirement first based on measured individual component draw and then determined the battery specifications and weight. Then I estimated the total weight and size of the unit from existing part weights/sizes and added estimates of additional parts.

Purpose

The work in this report offers a concept of a portable EV profound hypothermia induction unit and a feasibility study on the practicality of the concept.

Description of Apparatus and Setup

N/A

Summary of Data and Results

Considering information provided in Reference 2 above, I developed the table shown in Figure 1 and determined the total current draw required to be 5 A worst case when the compressor is turned on. However if pre-chilled fluid is used the compressor will not be on all the time (say 50% of the time). Also when the pump starts up the compressor will be automatically turned off (note that the fluid will remain cold even with the compressor off over the course of the procedure due to insulation). All these reduce battery requirements to 3.2 A and extend battery operation. Using information provided in Reference 3., I recommend a Panasonic battery model LC-RD1217P (rechargeable, sealed lead acid, 14.3 lbs, 7"X3"X6.6") that provides 17 Ah (20h rate).

Component	Current Drawn from 12V Battery (A)
Fan	0.80
Electronics	0.50
Pump at 2 L/min	1.40
Compressor	3.70
Total	5.00

FIGURE 1

Considering information provided in Reference 1 and the weight of the battery, I formed the table shown in Figure 2. The predicted total weight will be 61.3 lbs, for aluminum frame and panels. However if plastics are used for the panels, cooling chamber, and parts of the frame, the total weight may be reduced by about 10 lbs.

Component	Weight (lbs)
Battery	14.3
Electronics/controls	1.00
Pump/Motor	8.00
Compressor/condenser	12.50
Evaporator	1.50
Cooling Chamber	5.00
Frame	15.00
Panels	4.00
Total	61.30

FIGURE 2

The sizes of the major individual units are shown in the table of Figure 3. These could be packaged in a unit of size 2.5ft x 3ft x 1ft.

Component	Size (HxWxD)
Battery	7" x 3" x 6.6"
Electronics	6" x 8" x 1"
Pump Motor	8.8" x 3" x 4.5"
Compressor/Condenser	8" x 5.2" x 4.8"
Evaporator	14" x 10" x 1"
Cooling Chamber	24" X 20" X 10"

FIGURE 3

Conclusions

A portable profound hypothermia induction device as described will weight about 105 lbs when filled with 20 L of fluid, will be packaged in an enclosure that is 2.5ft x 3ft x 1ft or less, and will be good for 6 hours of operation and for 1 hour of pump operation when the battery is fully charged.

Suggestions for Further Work

No further work is necessary.

Appendix Q

ARDIEM

DESIGN REQUIREMENTS DOCUMENT

Profound Hypothermia Induction Device for EV

Program No. 2004-02

Revision X00, Effective 06-25-2004

Contents

1. Product Functional Requirements

1.1 Maintainability Requirements

1.2 Operational Requirements

1.2.1 Intended Use

1. The device is to be used for the induction of profound hypothermia in an emergency vehicle or any setting public or private even in the battlefield. Profound hypothermia is induced by initiating a rapid one-way flush with a large volume (10 or more liters) of cold solution via a specialized catheter.
2. The device will be applicable to 95% of children, adolescent, and adult population as defined in the AAMI / ANSI HE74-2001 Human factors design process for medical devices.

1.2.2 Physical Description

1. The device will be housed in a framed enclosure and consist of an inner cooling chamber capable of holding one filled 20-liter fluid bag of sterile solution, a refrigeration system, a pumping system, custom electronics, inputs and readout for patient temperature sensors, bubble detector, tubing occluder, and a disposable infusion set.
2. The disposable infusion set will consist of fluid bag, 1 m long L/S-18 tubing, a bubble trap/filter.
3. The device will be movable with wheels for ease of movement such that a single individual can maneuver it.
4. The device will have handles to allow lifting and moving on/off a vehicle or moving up/down stairs.
5. The device weight will be a maximum of 45 kg when loaded with fluid.
6. The device dimensions will be a maximum of 75 cm X 50 cm X 30cm (H X W X D).

1.2.3 Operating Modes

The device will be loaded with a bag of pre-chilled fluid and be powered on.

1.2.3.1 Standby Mode

1. The device will aim to maintain the chilled fluid at $0^{o}C \pm 0.5^{o}C$.
2. The device will monitor temperatures and display the fluid temperature and the patient temperature.

1.2.3.2 Flush Mode

1. In this mode the device will deliver the fluid through the disposable tubing-set and catheter to the patient at a fixed nominal rate of 2 L/min. Note that the catheter (3mm bore x 1.5 meter long) is not a part of the device.
2. The operator will install and prime the tubing by turning the pump on as needed then off.
3. The operator will hook up the tubing to the catheter and turn the pump on to start the cold flush.
4. The device will detect when nearly all the fluid is dispensed and turn the pump off.
5. The operator may turn the pump off and restart it at any time.
6. The device will keep monitoring temperatures and display the fluid temperature and the patient temperature.

1.2.4 Operator Interface

1.2.4.1 The operator input interface will consist of a means of selecting the following parameters:

1. Device power on/off.
2. Pump on/off.
3. A means for connecting the tubing-set pump section and connecting to the fluid bag.

1.2.4.2 The device output to the operator will consist of the following:

1. Device power on/off indicator (RED).
2. Device Alert indicator (YELLOW).
3. Fluid and Patient temperature display.

1.2.5 Training

1.2.6 Verification and Validation

1.3 Quality Requirements

1.3.1 General

1.4 Repairability Requirements

1.4.1 General

1.4.2 Verification and Validation

2. Product Performance Requirements

2.1 Durability Requirements

2.1.1 Shock and Vibration

1. Shipping The device will withstand normal levels of shock and vibration without incurring functional damage when in the shipping configuration in accordance with ISTA Procedure 1B.

2.1.1.2 Handling

1. The device will withstand, in the uncrated configuration, hitting walls and other fixed obstacles at a walking speed and moving in and out of elevators and over thresholds at walking speed.

2.1.1.3 Solvents and Fluids

1. All exposed surfaces will be resistant to damage from commonly used hospital/clinical cleaning fluids (such as alcohol and 10% bleach) and contact with salts, bodily fluids, and glucose solutions.

2.1.1.4 RFI and EMI

1. The device will meet the RFI and EMI immunity requirements listed in 2.2.1 1-4

2.1.1.5 Verification and Validation

2.2 Environmental Requirements

2.2.1 EMC Requirements

1. Medical Electrical Equipment EMC: EN 60601-1-2: 2001
2. Radiated and Conducted Emissions: EN 55011: 1998 +A1: 1999 +A2: 2002, FCC Part 15
3. Electrostatic Discharge Immunity: EN 61000-4-2: 1995 +A1: 1998 +A2: 2001
4. Radiated Electromagnetic Field Immunity: EN 61000-4-3: 2002 +A1: 2002
5. Electrical Fast Transient / Burst Immunity: EN 61000-4-4: 1995 +A1: 2001 +A2: 2001
6. Surge Immunity: EN 61000-4-5: 1995, +A1: 2001
7. Power Harmonics, EN 61000-3-2: 2000
8. Voltage Fluctuation (Flicker): EN 61000-3-3: 1995, +A1: 2001

2.2.2 Operating Requirements

1. Ambient Temperature: 10°C to 40°C (IEC601-1, Section 10.2.1a)
2. Relative Humidity: 30% to 75% (IEC601-1, Section 10.2.1b)
3. Atmospheric Pressure: 525mm Hg to 795 mm Hg(IEC601-1, Section 10.2.1c)

2.2.3 Storage Requirements

1. Ambient Temperature: -40°C to 70°C (IEC601-1, Section 10.1a)
2. Relative Humidity: 10°% to 100% max non-condensing relative (IEC601-1, Section 10.1b)
3. Atmospheric Pressure: 525mm Hg to 795 mm Hg (IEC601-1, Section 10.1c)

2.2.4 Verification and Validation

2.3 Performance Requirements

2.3.1 Electrical Requirements

2.3.1.1 Electrical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with UL 26601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety.
2. Use relevant components that are approved by at least one agency.

2.3.1.2 Power

1. Battery Voltage: 12 VDC +/-10%
2. Battery Current: 5 A
3. Battery Capacity: 10 Ah

2.3.1.3 Verification and Validation

2.3.2 Electronic Requirements

2.3.2.1 Central Processing Unit

1. Use a central processing unit (CPU) to control the overall operation of the device, including data acquisition, electro-mechanical components, operator interfaces, and communications interfaces.
2. Provide the capability to reset the CPU without cycling power off and on.

2.3.2.2 Real-Time Clock

1. Maintain the device's total operation time over its life.
2. Use a real-time clock (RTC) to associate a specific date and time with each reported measurement.
3. The RTC will continue to operate in the absence of power.

2.3.2.3 PCBAs

1. Design the device with no more than three (3) PCBAs.

2.3.2.4 Operator input

The operator will input the following data:

1. Power on/off will be initiated by a switch
2. The pump will shut down immediately when the operator switches to off.

2.3.2.5 Operator output

The following data will be output from the device:

1. A light indicator will indicate that power is on.
2. The fluid temperature will be displayed in °C on an LCD with an accuracy of ±0.3°C over the range of –10°C to 40°C.
3. The patient temperature will be displayed in °C on an LCD with an accuracy of ±0.3°C over the range of -10°C to 40°C.

2.3.2.6 Device diagnostics

1. The electronics will enable device diagnostics.

2.3.2.7 Safety limits

1. The electronics will detect the existence of bubbles in the extra-corporeal circuit fluid that are greater than 20μL and automatically activate the occluder, shut down the pump, and display a warning message for the condition. The device will then prompt and require user input to either resume operation or enter Cooling Mode.

2.3.2.8 Verification and Validation

2.3.3 Embedded Software

2.3.3.1 General

1. Control overall system operation.
2. Invoke operator input.
3. Provide operator output.
4. Control temperature.

2.3.3.2 Data Collection, Processing, and Relaying

1. Acquire temperature, and other data.
2. Save all data temporarily with time stamps.

2.3.3.3 Test and Diagnostics

1. Perform tests to detect faults.
2. Save faults until interrogated over serial interface.

2.3.3.4 Safety limits

1. The software will turn on alert indicator if the fluid temperature drops below $-1^{\circ}C$.
2. The software will turn on alert indicator if the tympanic patient temperature drops below $9^{\circ}C$.
3. The software will shutdown the pump when the total volume of the fluid is dispensed.

2.3.3.5 Verification and Validation

2.3.4 Mechanical Requirements

2.3.4.1 General

1. Provide easy access to cooling chamber.
2. Provide easy access to the pump head.
3. Provide easy access to sensor inputs (temperature).
4. Provide easy access to the operator interface.

2.3.4.2 Thermal Requirements

1. Isolate the electrical/electronics compartment from the refrigeration compartment.
2. Limit the internal device temperature to 40°C under normal operating conditions.
3. Limit the cooling chamber heat-loss to $2^{\circ}C$/hour under normal operating conditions.

2.3.4.3 Mechanical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with the mechanical safety requirements of UL 60601-1 Medical Electrical Equipment, Part 1: General Requirements

for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety. Also, design and manufacture the device to comply with safety requirements for specific components or systems, such as refrigerating systems (ISO 5149:1993 Mechanical refrigerating systems used for cooling and heating – Safety requirements, and ASHRAE Standard 15-2001 – Safety Standard for Refrigeration Systems), fan guarding (ISO 12499:1999 Industrial fans – Mechanical safety of fans – Guarding), and electromechanical relays (IEC 61810-1:2003 Elementary relays -- Part 1: Safety and general requirements).

2.3.4.4 Verification and Validation

3. References

00000-XX Title of document [Reference Style]

4. Revisions

Rev.	Description	Author	Effective Date
X00	Preliminary Issue	Mike Pitsakis	6-25-04

Appendix R

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00016

TITLE OF TECHNICAL REPORT			REVISION
Temperature Loss Comparison with several types of insulators.			0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER		DATE
Hypothermia	2004-02		06/16/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT		NAME OF AUTHOR	
Insulating comparisons.		Christina Park	

TECHNICAL AREA

Test, Measurement

SUBJECT AND KEY TECHNICAL WORDS

Hypothermia, insulating comparisons

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☒ Other

ASSOCIATED REPORTS

Abstract

The Profound Hypothermia Induction device prototype has proven in past tests that it had a very good insulating value. A second device has now been completed and it needed to be retested to verify its insulating quality as well. Other products were also tested for their insulating value, in comparison to the profound unit, in an effort to move closer to the goal of having a portable profound hypothermia device. The insulating material used in the Arctic Zone cooler performed the best and should be considered for deployment.

Background

Profound hypothermia can be used in trauma-induced exsanguinations cardiac arrest or cardiac arrest, which cannot be reversed by defibrillation. In these cases, which are considered unresuscitable by standard advanced life support procedures, the profound hypothermia (suspended animation), with or without drugs, is intended to preserve the viability of targeted organs until surgical repairs and delayed resuscitation can be performed. The induction of profound hypothermia is accomplished by a rapid large volume cold flush via a specially designed, occluding, aortic balloon catheter (developed under a separately funded program) placed in the thoracic aorta. The flush rapidly cools the heart and brain initially, then the abdominal organs with the collapse of the catheter-occluding balloon. Cooled fluid and diluted blood may or may not be recirculated depending on the scenario.

Introduction

The second prototype of the Profound Hypothermia induction device was constructed and tested. The device uses a vapor-compression refrigeration cycle and a custom designed cold box for cooling or maintaining the fluid contained in a standard 10 L hospital bag. Temperature control was accomplished by electronically cycling the compressor on/off. With this unit being completed, the quality of the insulation on the unit needed to be tested. Other means of insulating the pre-chilled fluid bags also needed to be considered for future uses as a portable / battlefield device.

Purpose

The quality of the insulating factors presently in the Profound Hypothermia device needed to be tested to verify the unit would be able to maintain the temperature of a pre-chilled bag for several hours, even if the unit was no longer running. For future uses, the device needs to be portable by one individual out in the battlefield, so other means of insulating the fluid bag also needed to be explored.

Description of Apparatus and Setup

The device was designed to monitor two patient temperatures (Patient 1 and Patient 2), Inflow (to the patient), Outflow (from the patient), internal ambient (inside the unit), heat exchanger (primary), and record these temperatures every three seconds via a computer. This communication was possible through a serial link connecting the device to a laptop computer and using the HyperTerminal program. The data recorded by the computer is saved as a text file, which is then converted using the extract.tcl program. The data is then converted into a new format, which sets the data up into columns, making the information more easily viewed using an Excel spreadsheet. The Stein-Hart model is used by software to convert resistance readings to temperature (calibrated between -15°C to 45°C). YSI #44004 temperature sensors were used (2252 @25°C, thermistor Mix "B") for temperature measurement. These sensors have an accuracy of ±0.2°C from 0°C to 60°C and ±0.1°C from 32°C to 42°C (Yellow Spring Instruments data sheets). The measurement error can be attributed to the 0.1% resistor sensor interface circuit, the 12-bit A/D, and the conversion routine, which adds another ±0.1°C to the error (according to the model/simulator spread sheet Mod_Therm YSI.xls).

Summary of Data and Results

The first test used a pre-chilled 10L fluid bag, which was inserted into a styrofoam cooler. The temperature change was then recorded over a period of a few hours. The data was plotted and shown in Figure 1. The Styrofoam cooler was found to have a heat loss rate of 1.20°C/hr.

The second test used a pre-chilled bag and the cold box of the device chilled down to 10°C. Once the set point temperature was accomplished, the device was turned off and the temperatures (Patient 1, Patient 2, Inflow and Outflow) were recorded for several hours. The data was plotted and shown in Figure 2. The device with a pre-chilled bag was found to have a heat loss of 1.40 °C/hr.

The third test setup used a pre-chilled 10L fluid bag and an Arctic Zone soft-sided portable cooler, without its plastic insert. The bag was inserted into the cooler and the temperature loss was recorded for several hours. The data was plotted in Figure 3. The setup was found to have a heat loss of 0.77°C/hr.

The fourth test setup also used the Artic Zone cooler, but the plastic insert was replaced. The test was run again using a pre-chilled bag and the data was plotted in Figure 4. The cooler with its plastic insert was found to have a heat loss rate of 0.73°C/hr.

The fifth test setup again used the Artic Zone cooler without it's plastic insert. The setup also used a frozen freezer pack, inserted into the bottom of the cooler. The pre-chilled bag was placed into the cooler and the heat loss was recorded over several hours. The data was plotted in Figure 5. The heat loss for the setup was found to be 0.63°C/hr.

The resulting data is summarized in the table shown in Figure 6.

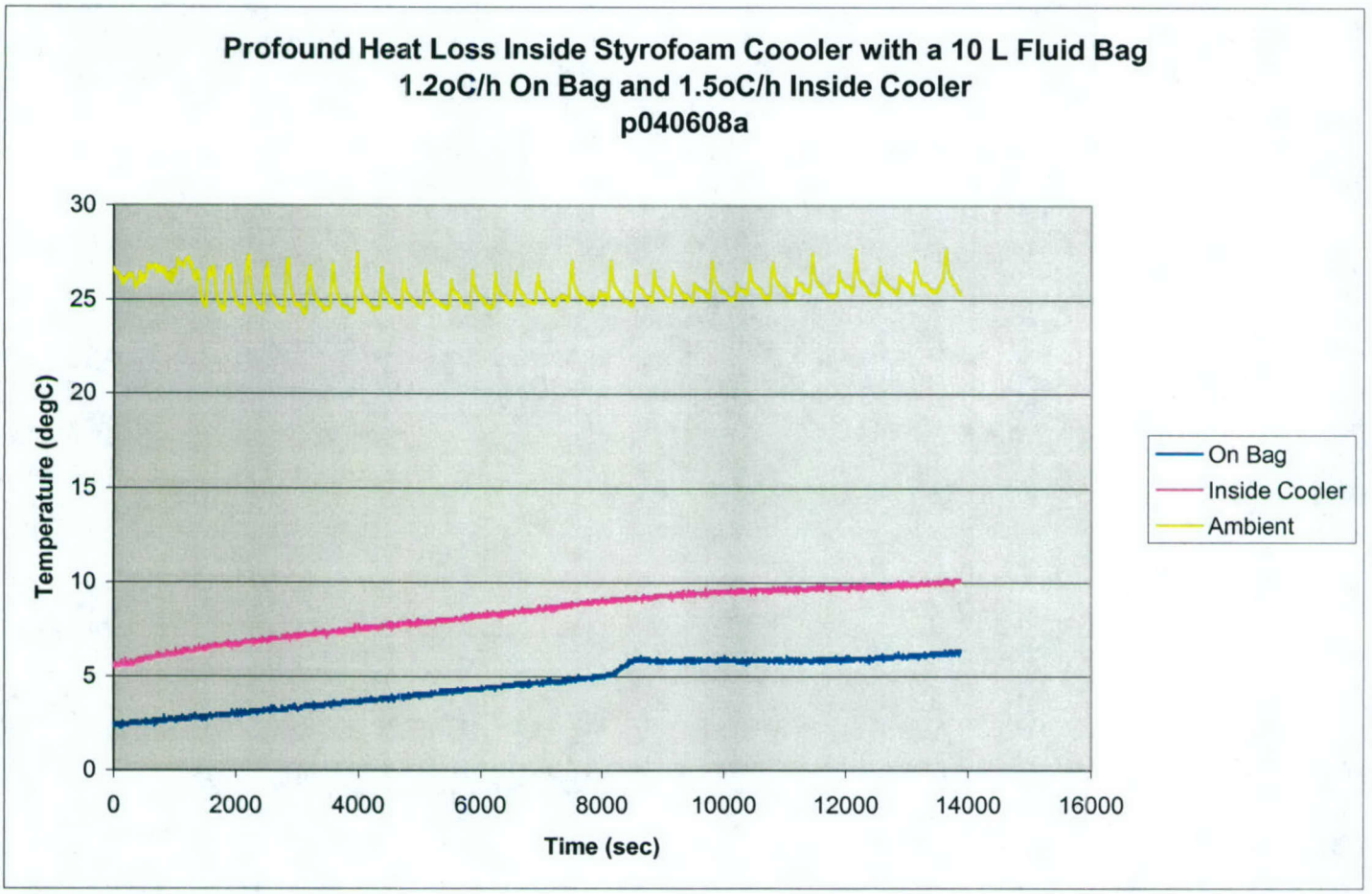


FIGURE 1

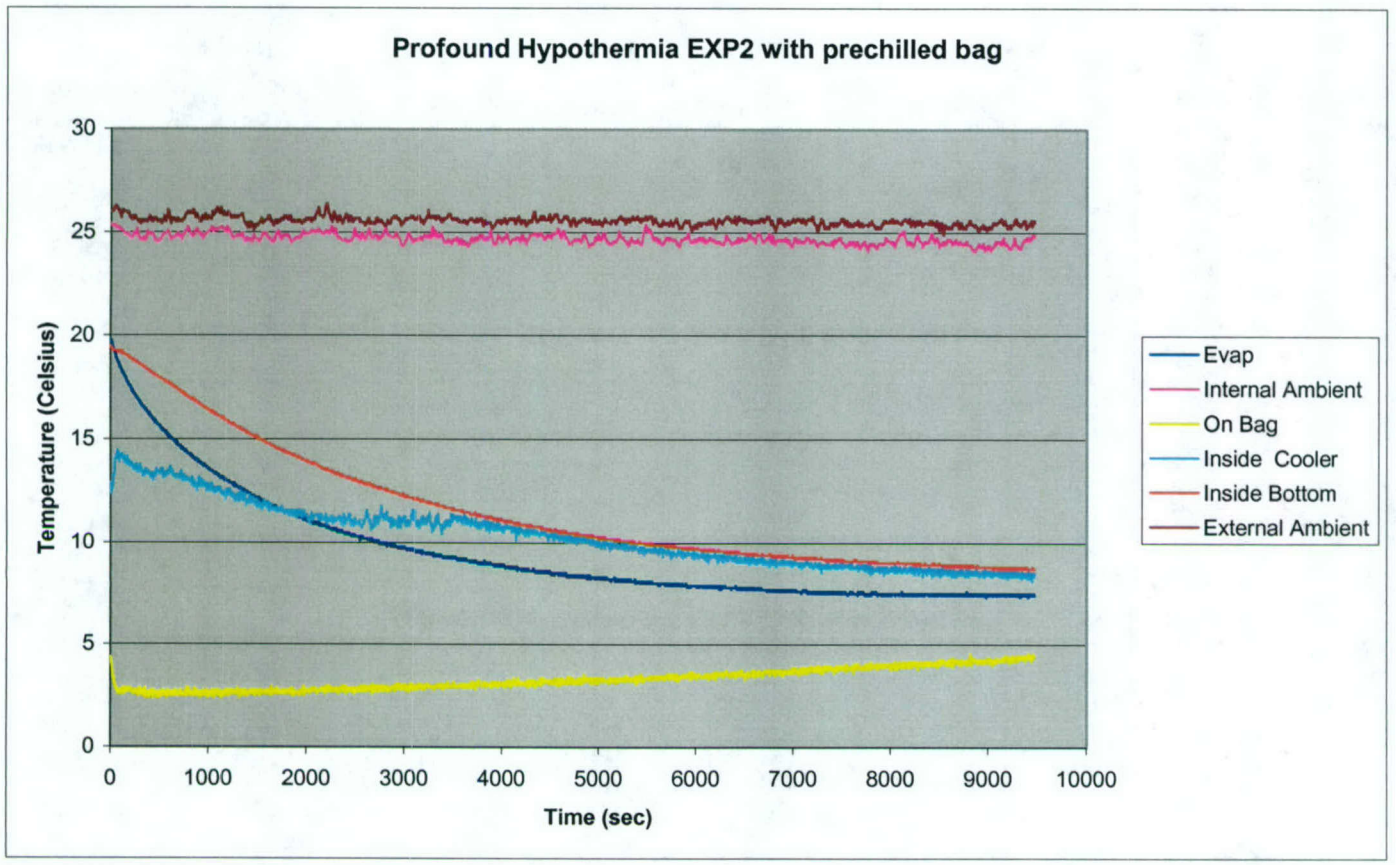


FIGURE 2

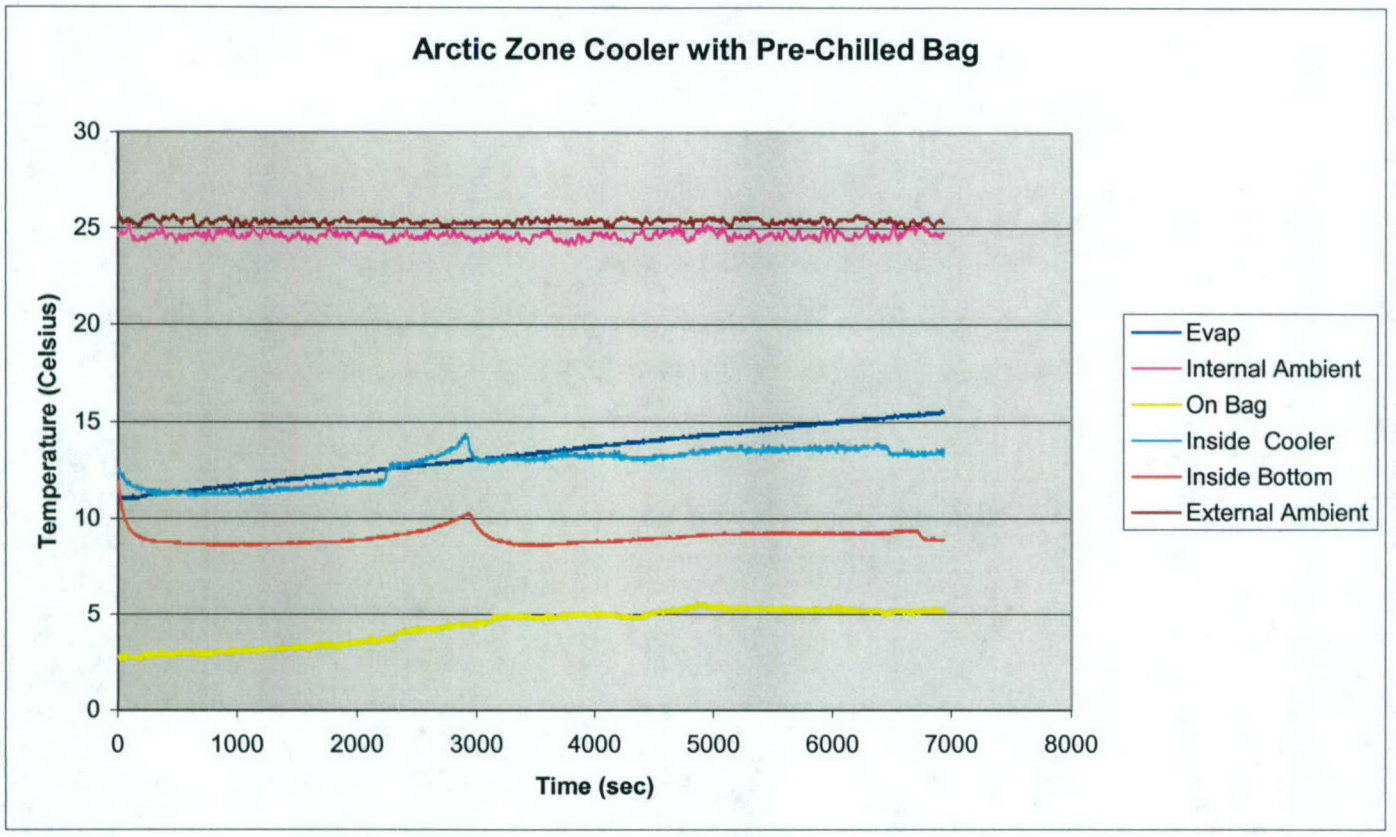


FIGURE 3

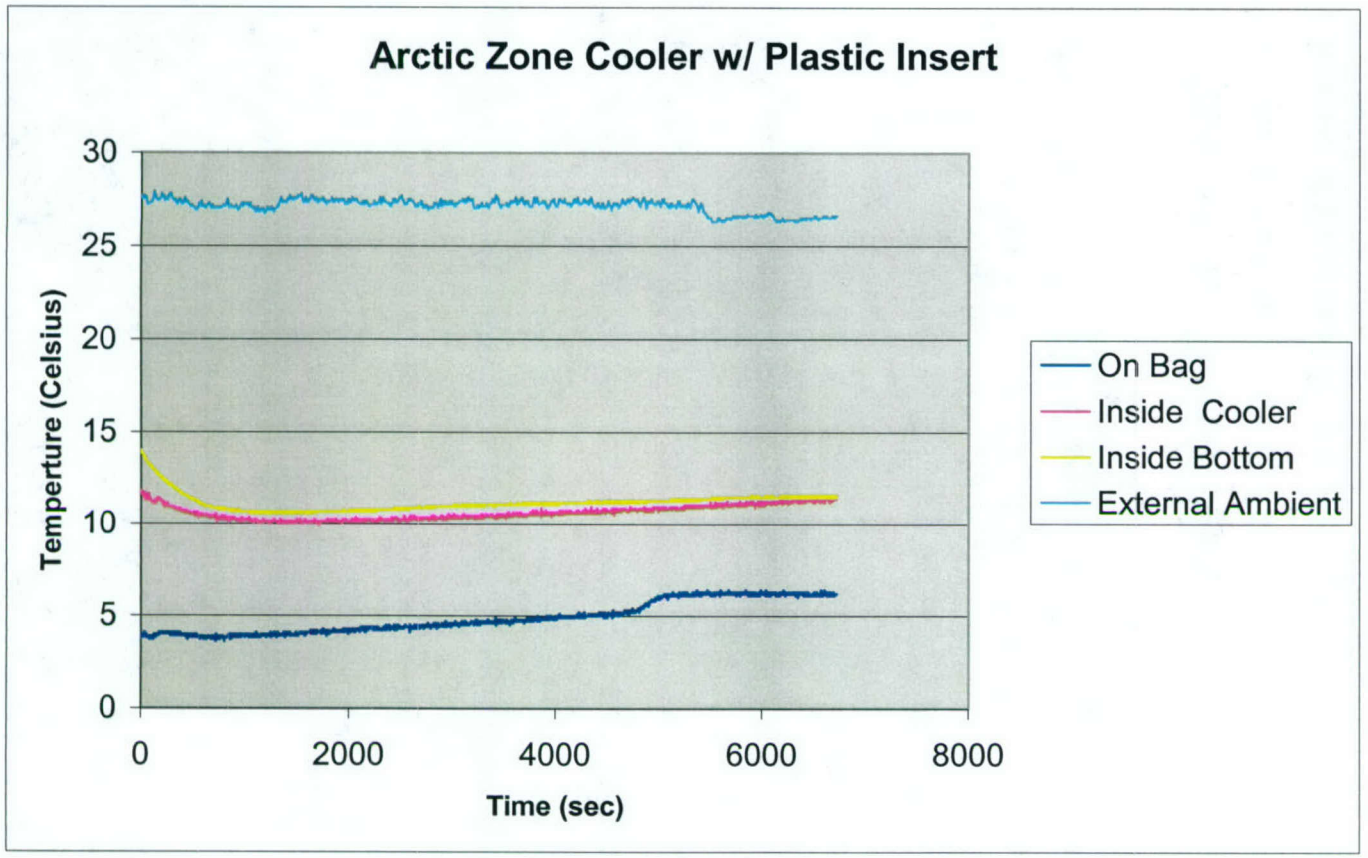


FIGURE 4

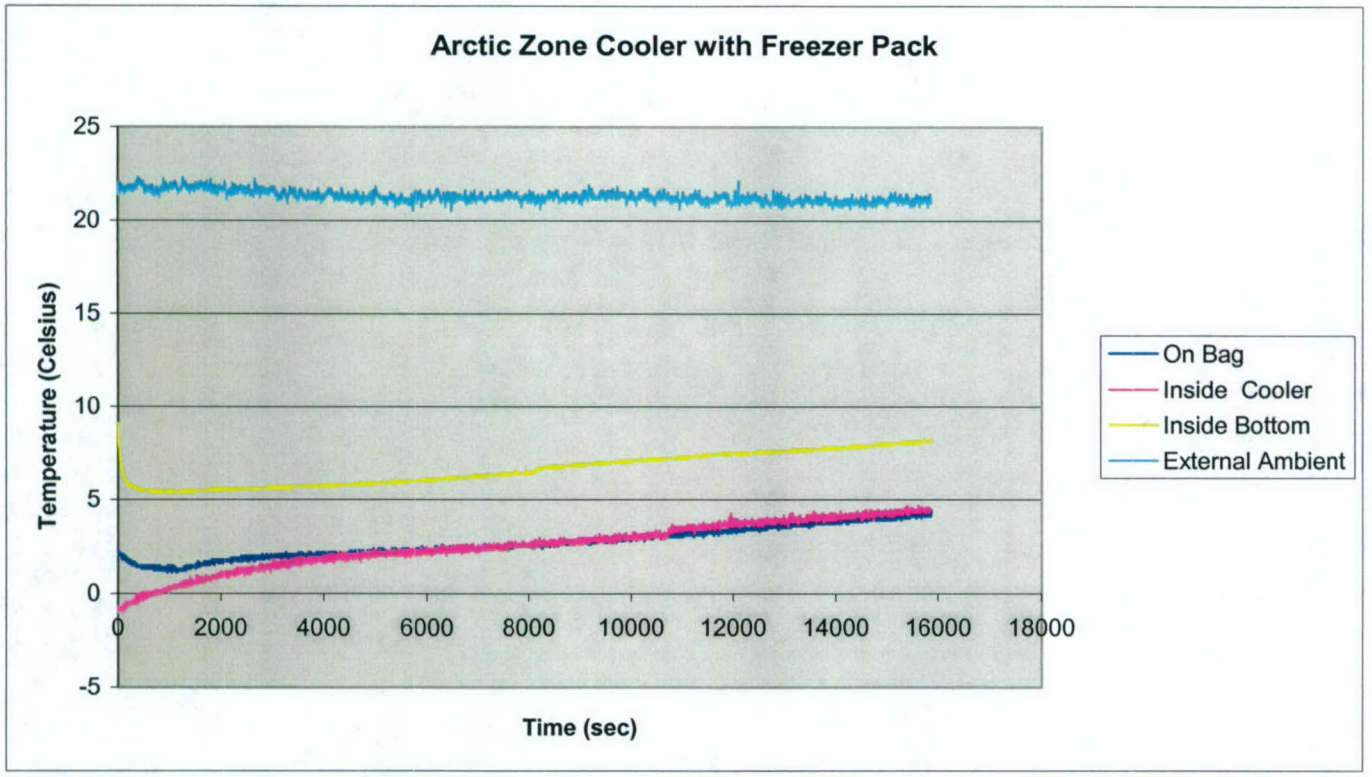


FIGURE 5

file name	description	rate (degC/h)
p040608a	styrofoam container	1.20
p040609b	EXP2	1.40
p040609c	cooler bag w/ plastic container	0.73
p040609d	cooler bag w/o plastic container	0.77
p040611a	cooler bag w/o plastic container and with a freeze pack	0.63

FIGURE 6

Conclusions

The best heat loss was found using the Arctic Zone cooler, without its plastic insert, and a frozen freezer pack inserted at the bottom of the cooler. This translates to about 8 hours of usable fluid for a cold flush assuming the starting temperature of the pre-chilled fluid is 0°C and 5°C fluid can induce rapid profound hypothermia. The heat loss in this test setup was less than half that found using the Profound Hypothermia device, EXP2. Although the heat loss in all the test setups was found to be fairly minimal, the information clearly shows that there are better ways to insulate the cold box.

Suggestions for Further Work

More heat loss testing may need to be done on other cooler units to decide which insulating factors will work the best for the portable / battlefield application.

Appendix S

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00017

TITLE OF TECHNICAL REPORT		REVISION
Combat Profound Induction Device Concept and Feasibility		0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-02	6/17/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
	Mike Pitsakis	

TECHNICAL AREA

SUBJECT AND KEY TECHNICAL WORDS

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

Abstract

I present a concept and feasibility study for a combat portable profound hypothermia induction (SA) device. The unit will be housed in a back pack, weigh less than 70 lb including the weight of a 20 L bag filled with pre-chilled fluid, and will operate on battery power with simple controls. The fluid will stay cold enough to perform an operation for six or more hours, and the battery will provide power for up to 100 minutes of pumping fluid.

Background

The following information contained in the technical reports listed below under References is available. The information pertains to profound hypothermia induction devices that we can apply to determine feasibility of a combat-portable unit.

References

1) Technical report "Hypothermia Induction Engineering Considerations", TR_Hypo 030606 MP.doc, provides information regarding cold flush liquid volume and time required to reduce core body temperature based on spreadsheet simulation Calc_Hth 0.xls. Relevant results are summarized in the table shown in Figure 1 below.

At 2 L/min		80 kg			Heart-Brain	
Initial fluid temp. (oC)	0	5	0	5	0	5
final body temp (oC)	20	20	26.9	28.3	20	20
volume of fluid required (L)	45.3	60.4	20	20	1.2	1.6
time required (min)	22.6	30.2	10	10	0.6	0.8

FIGURE 1

2) Technical report "Military Load Limits for Individual Soldiers", TR_Hypo 030702 DM.doc provides information as to the weight requirements: "With the information provided in FM 21-18 and the projected use conditions, an emergency hypothermia device should weigh no more than 72 pounds in total for a single soldier to carry to the point of application. It is preferable to keep the device weight less than the recommended fighting load of 48 pounds but since, in application, it would only be carried a short distance, the higher load is feasible."
3) Technical report "Temperature Loss Comparison with several types of insulators", TR_Hypo 040616 CP.doc provides information regarding best lightweight insulations that were tested. "The insulating material used in the Arctic Zone cooler performed the best and should be considered for deployment". That is polyethylene foam ¼" thick insulation heat loss at room temperature is 0.77 °C/hr and 0.63°C/hr with a freeze pack (2.5 lbs and 7 ¼" X 7 ¾" X 1 ½").
4) Technical report "Hypothermia Induction Devices Electrical Power requirements", TR_Hypo 030708 MP.doc provides information regarding the power requirements for DC or AC operation.
5) Technical report "Energy Storage Devices for Possible Use in Portable Hypothermia Device", TR_hypo 030709 MP.doc, provides information regarding energy storage devices applicable for use in a portable hypothermia device.
6) Technical report "Profound Hypothermia Induction Prototype Device Weight Analysis" TR_Hypo 030916 RG.doc provides information regarding the weight of components comprising the first engineering prototype of the profound device and the overall weight. The peristaltic pump and motor weigh 8 lbs while the overall unit without fluid weighs 96.5 lbs.

Introduction

The basic requirements of a combat-portable hypothermia induction unit are lightweight and small enough for a soldier to carry to the battlefield, simple to operate in adverse conditions, and battery powered. The problem we encounter designing such a unit is the weight considering the large volume of fluid that is required.

Purpose

I present here a concept and a feasibility study of a combat profound hypothermia induction device.

Description of Apparatus and Setup

N/A

Summary of Data and Results

With regard to reference 1, an average weight soldier will require about 60 L of fluid for body temperature reduction to 20°C. This volume of fluid will weigh too much for the application. With regard to reference 2, the recommended weight is 48 lbs but considering that a 20 L (5.3 gallons) commercially available plastic infusion bag weighs 44 lbs by itself when filled with fluid (size W X H X D is 16" X 19" X 6"), and that it is impossible to constrain everything else to less than 4 lbs. Also with regard to reference 1, a) 20 L of fluid is the maximum volume acceptable weight wise, and minimum, operation wise (for body temperature reduction to 28°C), b) if only the heart-brain is to be cooled then volume is no problem, and c) ideally the colder the fluid the lower the required fluid volume will be, however, 5°C fluid is still usable.

With regard to reference 3, ¼" thick polypropylene or polyethylene foam is a good compromise primarily between thermal conductivity, specific gravity, durability and ease of use to be used for insulating the compartment of the fluid bag (see

Table shown in Figure 2). If the initial fluid temperature is 0°C, it will take 6.5 hours to rise to 5°C without a freeze pack and 7.9 hr with a freeze pack (at 25°C environmental).

Property	Polyurethane	Polyethylene	Polypropylene	Polycarbonate	Nylon	Teflon	Tefzel	Kynar
Thermal Conductivity (W/mdegC)	0.02-0.03	0.42-0.5	0.12	0.19	0.2-.22	0.25	0.25	0.13
Specific Gravity	1.5	1.09	0.9	1.2	1.38	2.2	1.7	1.75
Maximum Service Temperature (degC)	65	100	100	100	110	260	150	150
Isod Impact Strength Notched (J/m)	430			908	107	160	NB	1068
Tensile Streangth at yield (MPa)	190	40		62	172	21	45	34
Flammability	UL94:94HB	UL1820	UL94:94HB	UL94:94V-2	UL94:94HB	UL94:94V-0	UL94:94V-0	UL94:94V-0

http://www.pspglobal.net/polyethylene.html
FIGURE 2

With regard to reference 4 and the assumption that only simple controls and electronics are required[1], the power requirements will be reduced significantly if we do not use refrigeration[2] and only need to power the pump motor[3] and electronics as summarized in the table shown in Figure 3.

SYS 3	Power (W) @ 12VDC	Draw (A) @ 12VDC
Electronics System	1.2	0.1
Pumping System	14.4	1.2
Cooling System	0	0
Total	15.6	1.3

FIGURE 3

With regard to the above table and reference 5, a PANASONIC battery model LC-R122R2P (UL listed, rechargeable, sealed lead acid), for example, offers 2.2 Ah at 1.8 Lb weight and small size (W X H X D) 7" X 2.4" X 1.4" and is good for 60 min of pump operation and 20h of standby operation.

With regard to reference 6, the total weight will be reduced tremendously if we pack everything using vinyl lining inside and some synthetic fabric outside, and a light aluminum frame and bottom support, as listed in the table shown in Figure 4.

Component	Weight (lbs)
Battery	1.8
Pump/Motor	8
Electronics/ controls in aluminum enclosure	1
Frame	5
Bottom support plate	1.5
Fabric case and insulation	3
Total	20.3

FIGURE 4

This will make the total weight 64.7 lbs without freeze packs and 69.7 lbs with two freeze packs, which is within 72 lbs.

Conclusions

A combat profound hypothermia induction device consisting of a framed back-pack made of vinyl, ½" polyethylene foam or even better ½" polypropylene foam, synthetic cloth, aluminum frame and bottom support that house a 20 L fluid bag with tubing and a catheter, a peristaltic fluid pump, a blood filter/air trap, a battery, and simple controls and electronics will weigh less than 70 lbs. It will be designed for quick set up of the disposable set, simple operation, and battery replacement. Refrigeration capability is not required and thus the excess weight of the refrigeration system will be avoided. The fluid volume will be limited to 20 L of 0°C pre-chilled saline solution or other solution that the Safar Center (SCRR) determines appropriate. The unit will be operated by a 12V rechargeable battery and include a switch to turn the pump ON/OFF (at 2 L/min), an LED to indicate battery charge OK, and another LED to indicate fluid temperature OK (< 5°C). The fluid will remain cold enough for a procedure for up to 6 hours. After 6 hours it will have to be replaced. The

[1] One switch for pump on/off, one LED indicator for battery OK, and one LED indicator for fluid temperature OK.
[2] Weight limitations prohibit the use of refrigeration. A suitable compressor would add 14 lbs plus require an additional 3.7 A from the battery which would also make the battery heavier and add another 6.6 lbs to overall weight.
[3] Unfortunate gravitational free flow of the fluid out of the bag (no pump) is limited by the catheter ID to about 0.26 L/min (note that L/S18 tubing limit is 2.7 L/min).

battery will last for at least the length of time required to pump the fluid (60 min) and then will have to be replaced by a charged battery. In standby mode (no pumping) the battery will last for 20h of operation.

Suggestions for Further Work

The assumptions and theoretical results must be evaluated by the SCRR for validity before a preliminary DRD is drafted and prototype design and fabrication work commences.

Appendix T

ARDIEM

DESIGN REQUIREMENTS DOCUMENT

Profound Hypothermia Induction Device for Combat

Program No. 2004-02

Revision X00, Effective 06-23-04

Contents

1. Product Functional Requirements

1.1 Operational Requirements

1.1.1 Intended Use

1. The device is to be used for the induction of profound hypothermia in the battlefield or anywhere. Profound hypothermia is induced by initiating a rapid one-way flush with a large volume (10 or more liters) of cold solution via a specialized catheter.

1.1.2 Physical Description

1. The device will be housed in a framed cloth back-pack and consist of an inner insulated chamber capable of holding a filled 20-liter fluid bag of sterile solution, a fluid pump, custom electronics, simple controls, and a disposable infusion set.
2. The disposable infusion set will consist of fluid bag 1 m long L/S-18 tubing, and a bubble trap/filter.
3. The device weight will be a maximum of 32 kg when loaded with fluid.
4. The device dimensions will be a maximum of 70 cm X 45 cm X 30cm (H X W X D).

1.1.3 Operating Modes

The device will be loaded with a bag of pre-chilled fluid.

1.1.4 Standby Mode

1. The device will maintain the chilled fluid between 0°C and 5°C ± 0.5°C.
2. The device will monitor the fluid temperature and battery voltage.

1.1.4.2 Flush Mode

1. In this mode the device will deliver the fluid through the disposable tubing-set and catheter to the patient at a rate of 2 L/min ±10%.
2. The operator will install and prime the tubing set by turning the pump on as needed then turn it off.
3. The operator will hook up the tubing to the catheter and turn the pump on to start the cold flush.
4. The operator will turn the pump off when almost all the fluid is dispensed.
5. The operator may turn the pump off and restart it at any time.
6. The device will keep monitoring the fluid temperature and battery voltage.

1.1.5 Operator Interface

1.1.5.1 The operator input interface will consist of a means of selecting the following parameters:

1. Pump on/off.
2. A means for connecting the tubing-set pump section and connecting to the fluid bag.

1.1.5.2 The device output to the operator will consist of the following:

1. Fluid Temperature OK. Indicator.
2. Battery OK indicator.

1.1.6 Training

1. Provide sufficient information in operator's manual.

1.1.7 Verification and Validation

2. Product Performance Requirements

2.1 Durability Requirements

2.1.1 Shock and Vibration

1. Shipping The device will withstand normal levels of shock and vibration without incurring functional damage when in the shipping configuration in accordance with ISTA Procedure 1B.

2.1.1.2 Handling

1. The device will withstand, in the uncrated configuration, hitting walls and other fixed obstacles at a walking speed and moving in and out of elevators and over thresholds at walking speed.

2.1.1.3 Solvents and Fluids

1. All exposed surfaces will be resistant to damage from commonly used hospital/clinical cleaning fluids (such as alcohol and 10% bleach) and contact with salts, bodily fluids, and glucose solutions.

2.1.1.4 RFI and EMI

1. The device will meet the RFI and EMI immunity requirements listed in 2.2.1 1-4

2.1.1.5 Verification and Validation

2.2 Environmental Requirements

2.2.1 EMC Requirements

1. Medical Electrical Equipment EMC: EN 60601-1-2: 2001
2. Radiated and Conducted Emissions: EN 55011: 1998 +A1: 1999 +A2: 2002, FCC Part 15
3. Electrostatic Discharge Immunity: EN 61000-4-2: 1995 +A1: 1998 +A2: 2001
4. Radiated Electromagnetic Field Immunity: EN 61000-4-3: 2002 +A1: 2002
5. Electrical Fast Transient / Burst Immunity: EN 61000-4-4: 1995 +A1: 2001 +A2: 2001
6. Surge Immunity: EN 61000-4-5: 1995, +A1: 2001
7. Power Harmonics, EN 61000-3-2: 2000
8. Voltage Fluctuation (Flicker): EN 61000-3-3: 1995, +A1: 2001

2.2.2 Operating Requirements

1. Ambient Temperature: 10°C to 40°C (IEC601-1, Section 10.2.1a)
2. Relative Humidity: 30% to 75% (IEC601-1, Section 10.2.1b)
3. Atmospheric Pressure: 525mm Hg to 795 mm Hg(IEC601-1, Section 10.2.1c)

2.2.3 Storage Requirements

1. Ambient Temperature: -40°C to 70°C (IEC601-1, Section 10.1a)
2. Relative Humidity: 10°% to 100% max non-condensing relative (IEC601-1, Section 10.1b)
3. Atmospheric Pressure: 525mm Hg to 795 mm Hg (IEC601-1, Section 10.1c)

2.2.4 Verification and Validation

2.3 Performance Requirements

2.3.1 Electrical Requirements

1. Means for measuring fluid temperature.

2.3.1.2 Electrical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with UL 26601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety.
2. Use relevant components that are approved by at least one agency.

2.3.1.3 Power

1. Battery Voltage: 12 VDC +/-10%
2. Battery Current: 1.3 A maximum
3. Battery Capacity: 2.24 Ah

2.3.1.4 Verification and Validation

2.3.2 Electronic Requirements

2.3.2.1 PCBAs

1. Design the device with no more than 1 PCBA.

2.3.2.2 Operator input

1. Pump on/off will be initiated by a switch

2.3.2.3 Operator output

1. Fluid Temperature OK indicator.
2. Battery OK indicator.

2.3.2.4 Verification and Validation

2.3.2.5 Data Collection and Processing

1. Monitor temperature of the insulated compartment. If over 50°C turn indicator off.
2. Monitor battery voltage. If less than 11.9 VDC turn indicator off.

2.3.2.6 Verification and Validation

2.3.3 Mechanical Requirements

2.3.3.1 General

1. Provide easy and fast access to insulated chamber.
2. Provide easy access to pump head.
3. Provide easy access to temperature sensor input.
4. Provide easy access to battery for quick replacement.
5. Provide easy access to operator interface.
6. Provide for easy mounting of the bubble trap/filter.

2.3.3.2 Form-factor

1. Design unit to be carried as a back-pack with aluminum frame.
2. Design unit to have three compartments: insulated compartment for the fluid bag (on top), compartment to hold tubing, bubble trap/filter, and catheter (middle), and compartment to hold pump motor, battery, and electronics box with aluminum sheet support (bottom).

2.3.3.3 Weight

Overall unit weight is limited to 22 lbs not including the fluid bag.

2.3.3.4 Thermal Requirements

1. Use ½ " thick lightweight polypropylene foam or polyethylene foam to insulate fluid bag.

2.3.3.5 Mechanical Safety

1. Design and manufacture the device to comply with product safety requirements of the United States of America and the European Community. This includes compliance with the mechanical safety requirements of UL 60601-1 Medical Electrical Equipment, Part 1: General Requirements for Safety (First Edition, replaces UL 2601-1), and EN 60601-1:1990+A1+A2+A13 Medical electrical equipment -- Part 1: General requirements for safety. Also, design and manufacture the device to comply with safety requirements for specific components or systems, such as refrigerating systems (ISO 5149:1993 Mechanical refrigerating systems used for cooling and heating – Safety requirements, and ASHRAE Standard 15-2001 – Safety Standard for Refrigeration Systems), fan guarding (ISO 12499:1999 Industrial fans – Mechanical safety of fans – Guarding), and electromechanical relays (IEC 61810-1:2003 Elementary relays -- Part 1: Safety and general requirements).

2.3.3.6 Verification and Validation

3. References

00000-XX Title of document [Reference Style]

4. Revisions

Rev.	Description	Author	Effective Date
X00	Preliminary Issue	Mike Pitsakis	23-06-2004

Appendix U

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00022

TITLE OF TECHNICAL REPORT		REVISION
The affects of using the Mild-to-Moderate device for both mild-to-moderate and profound hypothermia applications.		0
PROJECT OR PROGRAM NAME	**PROGRAM NUMBER**	**DATE**
Hypothermia	2004-03	07/02/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	**NAME OF AUTHOR**	
Verify the cooling capabilities of the Mild-to-Moderate device to achieve Profound Hypothermia results.	Christina Park	

TECHNICAL AREA

Test and Verification

SUBJECT AND KEY TECHNICAL WORDS

Hypothermia, Mild-to-Moderate Cooling Rate

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☒ Verification	☐ Product Support	☐ Risk Analysis	☐ Other

ASSOCIATED REPORTS

Abstract

A phase of the hypothermia project is to be able to incorporate both the mild-to-moderate hypothermia induction device and the profound hypothermia induction device into one unit. The current mild-to-moderate unit was setup to circulate 10L of fluid through the device at the maximum flow possible to simulate the profound device. The first test was run at a flow rate of 2 L/min. With such a high flow rate the heat exchanger did not have enough time to cool the fluid down so that the inflow temperature and outflow temperatures were not significantly different. The second test was run at a flow rate of only 1 L/min. This gave more time for the fluid to cool while passing through the heat exchanger, but it was not enough time to reach the desired temperature needed for the profound application. Neither Mild-Moderate prototype (Bench Top or Engineering 2) has enough cooling power to chill the fluid at the desired infusion rates sufficiently to induce profound hypothermia.

Background

It is a desire of the Safar Center to have one device that performs the functions of both the mild-to-moderate and profound hypothermia devices. Due to the complication of the electronics of the mild-to-moderate device, it was determined that it would be easier to modify this device to incorporate the profound hypothermia capabilities.

Introduction

The idea of combining both hypothermia devices (mild-to-moderate and profound) may be harder than originally thought. In order to perform the profound hypothermia induction, the fluid introduced into the body needs to be 0°C ±0.5°C. Without using a pre-chilled fluid bag, the current mild-to-moderate device may not have the capability to chill the fluid at a rate fast enough to induce profound hypothermia.

Purpose

The speed at which the fluid can be cooled using the mild-to-moderate hypothermia device is very important. If the device can cool the fluid to the desired profound hypothermia temperature quickly enough, the device can be successfully used for both applications.

Description of Apparatus and Setup

There were two devices used to perform this test. The first unit was the BenchProto. The BenchProto is a simplified version of the mild-to-moderate device. The second device used was the mild-to-moderate device itself. This device was designed to monitor internal ambient (inside the device), heat exchanger (primary), inflow (to the patient), outflow (from the patient), and two patient temperatures. The device records these temperatures and then reports them at three second intervals to a computer via a serial link. The data in the computer is saved in a text file containing time stamps of when the information was taken. The standard YSI #44004 (2252 @25°C , thermistor Mix "B") temperature sensors were used for temperature measurement. Masterflex 96440-18 (Platinum-Cured Silicone 3355L) tubing was used instead of the Masterflex 96420-25 (Platinum-Cured Silicone 3350) tubing normally used on the mild-to-moderate device to increase the flow rate. A 10L fluid bag, at ambient temperature, was filled with water and was used for the fluid flush.

Note that Inflow and Outflow temperatures in this report are with respect to the heat exchanger.

Summary of Data and Results

To determine the cooling rate of the BenchProto at ambient temperature, a disposable set was connected to the machine and a 10L bag of fluid was pumped through the system. The evaporator plates and fluid bag started at ambient temperature and the flow rate was set to 2 L/min. The temperature drop with this test set up was insignificant at only 4.2°C, as can be seen in Figure 1.

The cooling rate was then tested again using the BenchProto, and the evaporator plates were pre-chilled. The 10L fluid bag, at ambient temperature, was again pumped through the system. There was an improvement in cooling but not enough to initiate profound hypothermia. The data obtained can be seen in Figure 2.

The tests were then completed using a flow rate of 1 L/min in order to give the fluid more contact time with the evaporator plates. The results showed that the decreased flow rate improved the cooling rate much more than the 2 L/min. The test was performed again using the BenchProto with the bag and plates starting at ambient temperature. The results can be seen in Figure 3.

The procedure was repeated using the BenchProto with a 1 L/min flow rate, and a pre-chilled evaporator. The results were plotted and shown in figure 4. A temperature difference of 4.4°C was recorded.

The Mild-to-Moderate device was then tested using the same setup as the tests run on the BenchProto. The first test was run at 2 L/min and the fluid and evaporator plates were started at ambient temperature. The results can be seen in Figure 5. 19 psig of pressure were measured and a temperature drop of 5°C was recorded.

The Mild-to-Moderate device was tested again using a flow rate of 2 L/min, and the evaporator was pre-chilled. The results can be seen in Figure 6.

The device was then set to a flow rate of 1 L/min. The test was run with the bag and evaporator starting at ambient temperature. The results can be seen in Figure 7. When running the test the pressure was found to be within the tolerable range at 5.7 PSIG.

The final procedure was performed using the Mild-to-Moderate device. The flow rate was again set at 1 L/min, and the evaporator was pre-chilled. The pressure was found to be insignificant at 6.1 PSIG. The results can be seen in Figure 8. The fluid was cooled 6.1°C.

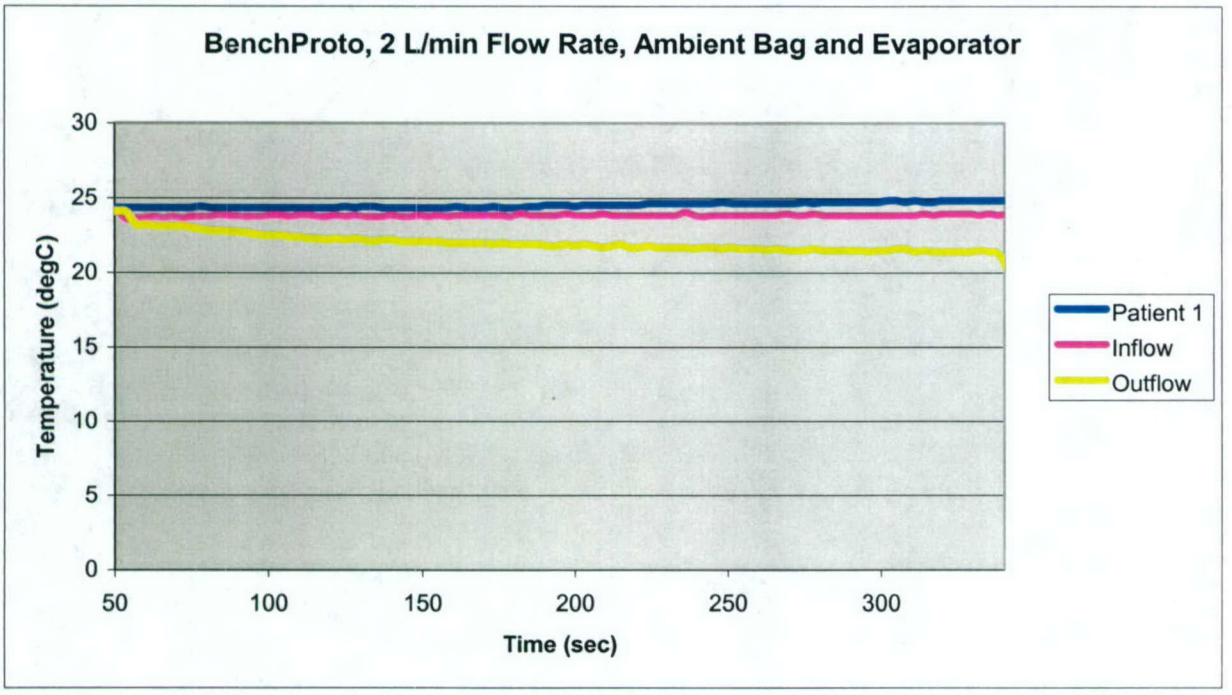


Figure 1

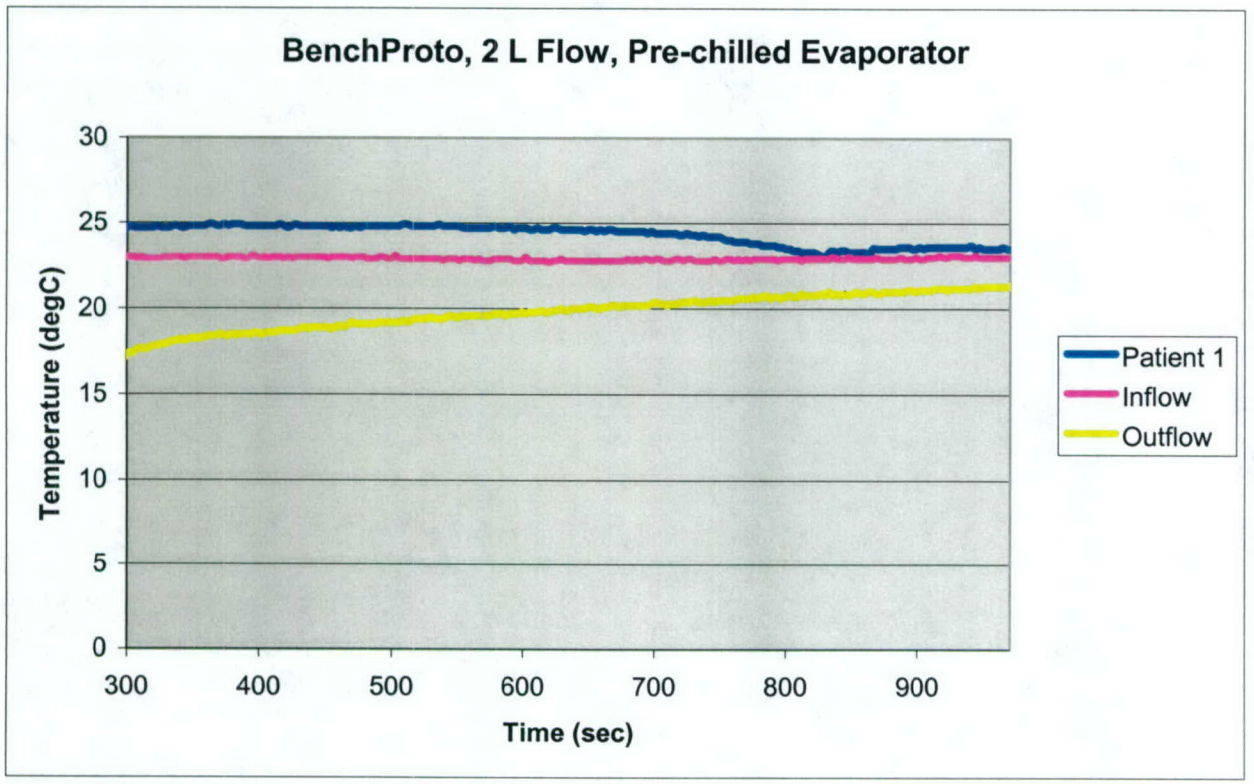


Figure 2

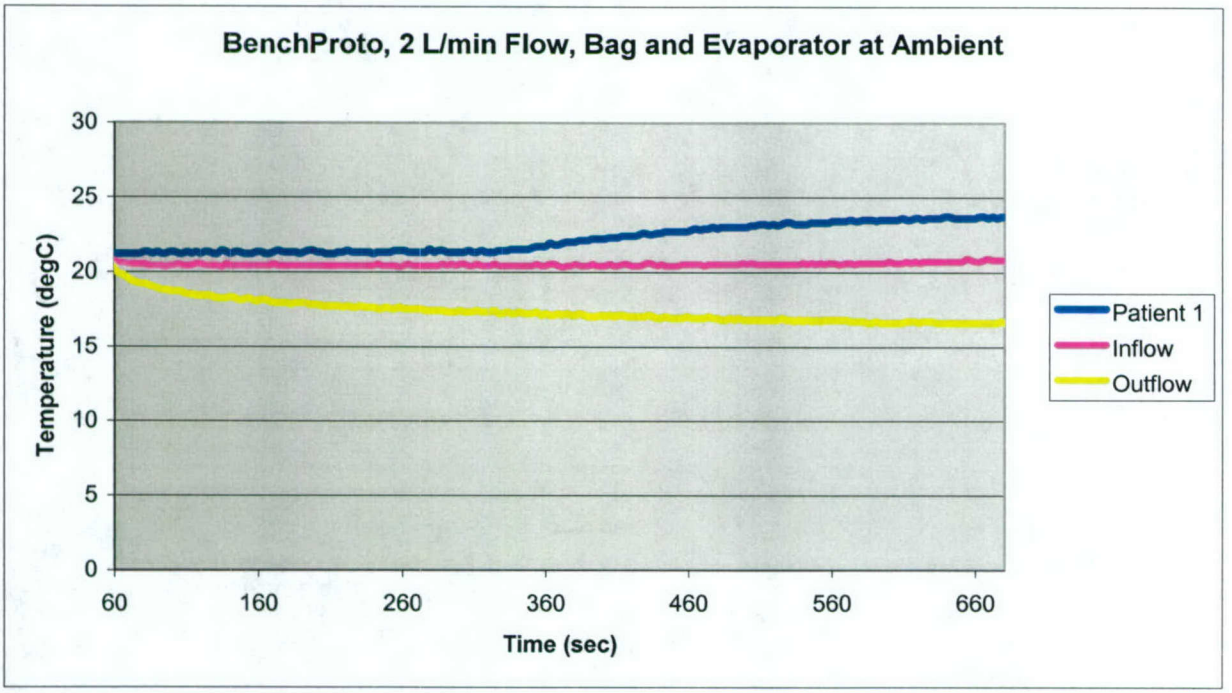


Figure 3

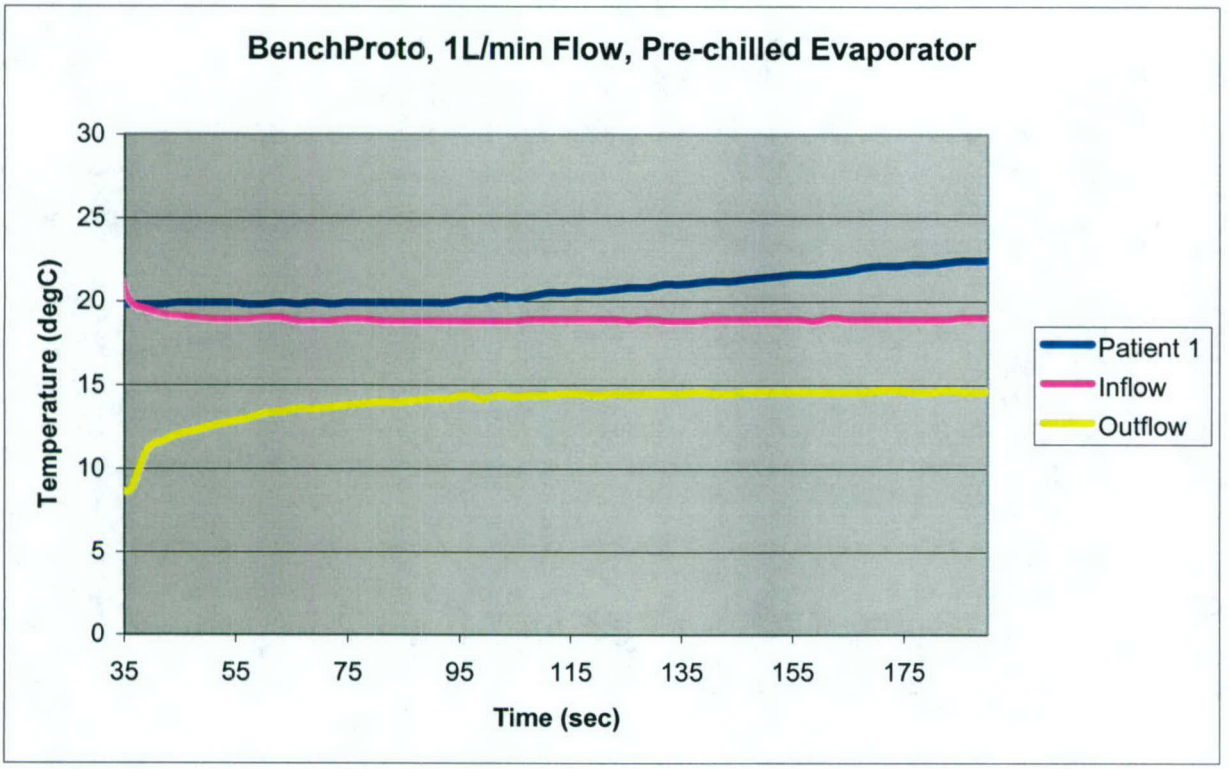


Figure 4

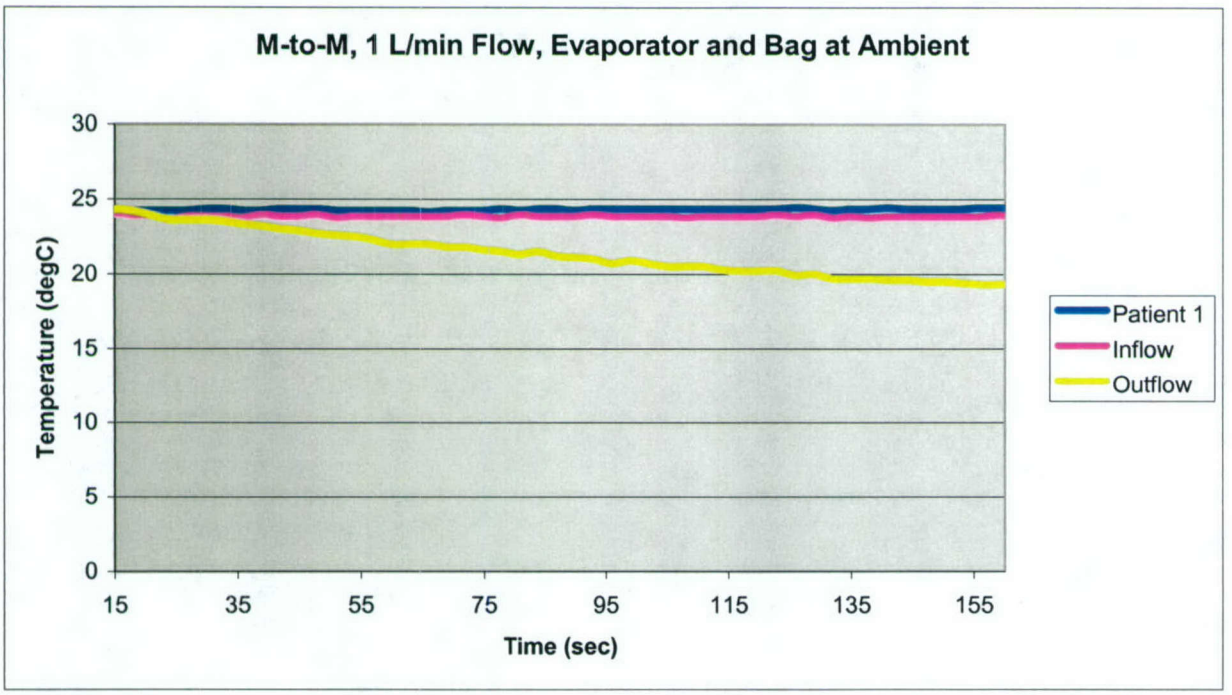


Figure 5

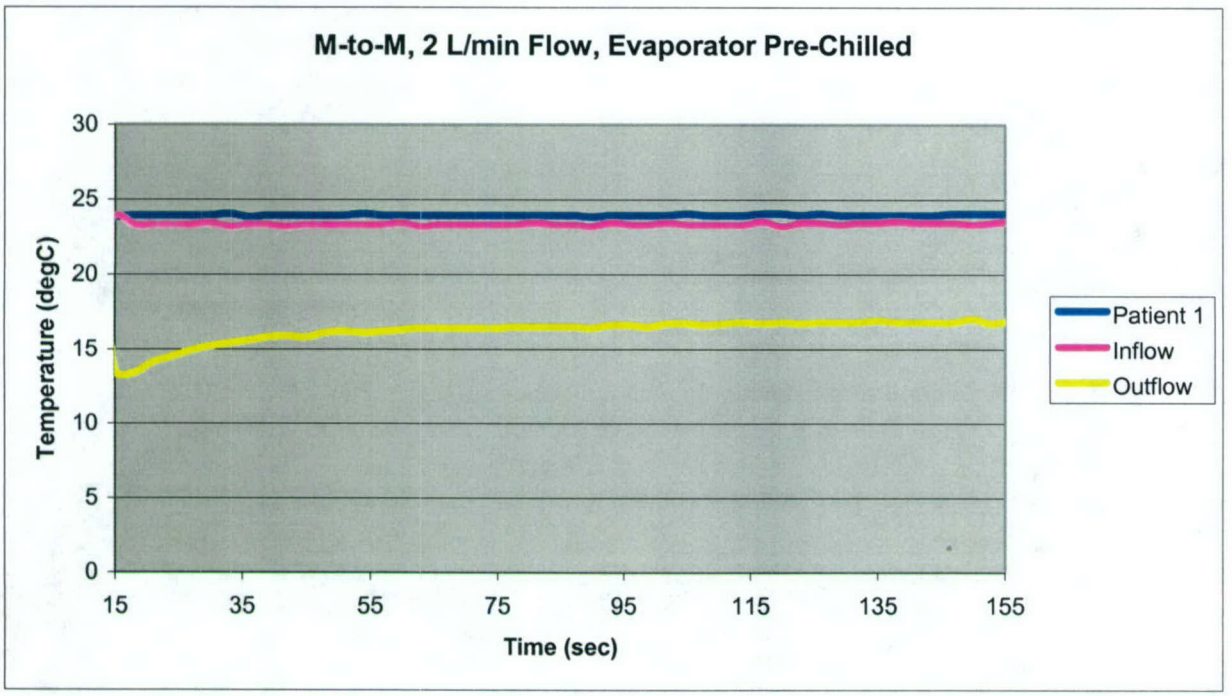


Figure 6

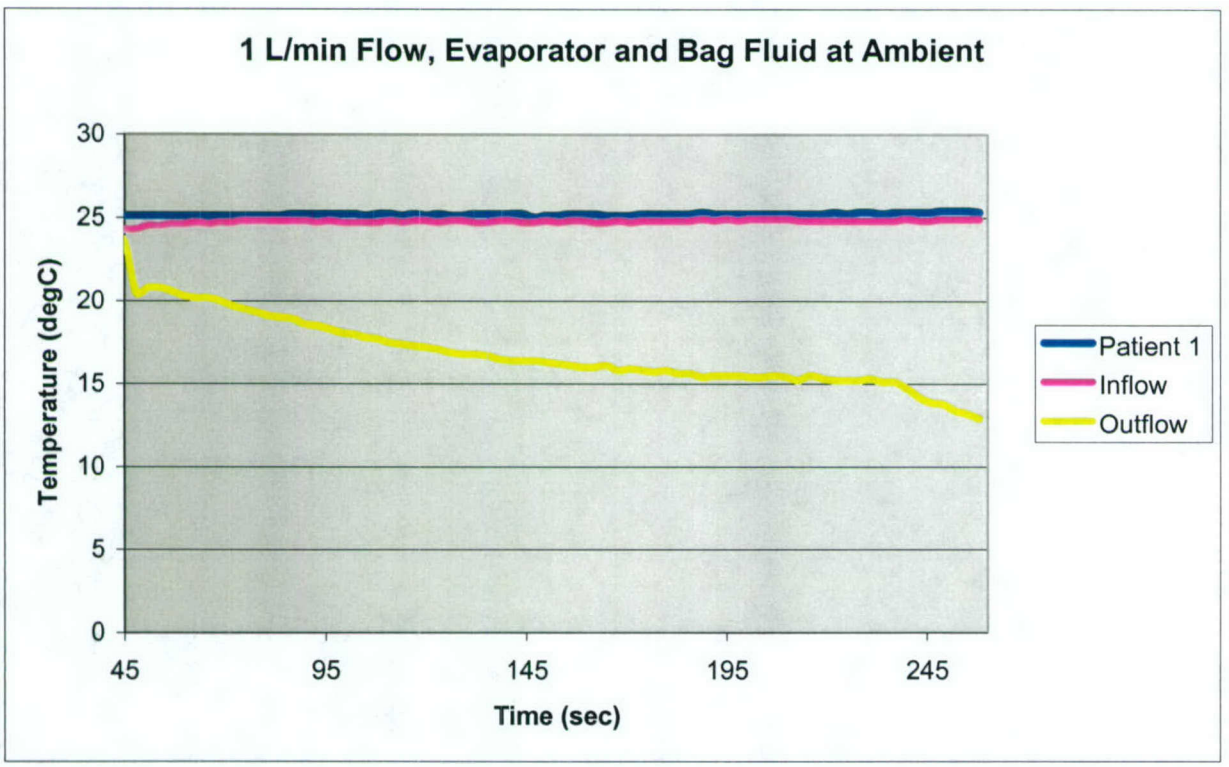


Figure 7

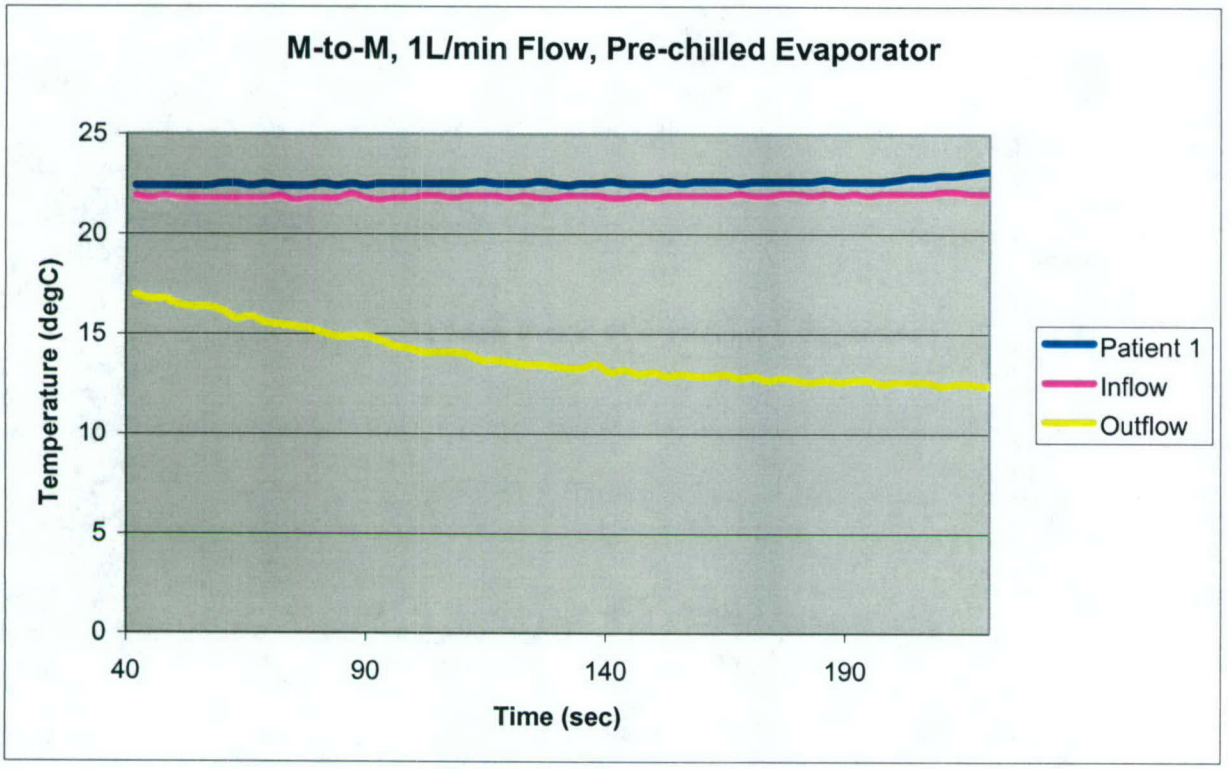


Figure 8

Conclusions

The best cooling rates were found using the 1 L/min flow rate and the pre-chilled evaporator. The 2 L/min flow rate did not give the device enough time to sufficiently cool the fluid to the desired temperature. When the evaporator was pre-chilled, the outflow temperature would appear to increase compared to the inflow temperature due to the warmer fluid (at ambient temperature) warming the evaporator plates. Again, timing is an issue here. If the unit had more time, these temperatures would equalize and the outflow temperature would again start to decrease.

Even with a cooling rate of up to 6.6°C, without modifications, the Mild-to-Moderate device is not capable of performing the cooling capacity required for Profound Hypothermia in such a restricted time frame (approx. 2.5 min. @ 2 L/min, and approx. 3 min. @ 1 L/min). The ideal induction of profound hypothermia uses 0°C fluid to chill the body immediately using a rapid, one-way fluid flush. Even with the mild-to-moderate's cooling capabilities, in the limited amount of time it takes to pump 10L of fluid through the system, the fluid is only at its maximum cooling temperature at the end of the procedure, not from the initial introduction, as the profound device does.

Suggestions for Further Work

More tests need to be done in order to have the mild-to-moderate device be able to perform both its own requirements and the requirements of the profound device.

Appendix V
TECHNICAL REPORT

Technical Report x.dot

RECORD NO.

AM-00008

TITLE OF TECHNICAL REPORT		REVISION
Thermodynamic Simulator of a Pig		0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Emergency Hypothermia	2003-01	12/05/03
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
Device Testing	Mike Pitsakis	
TECHNICAL AREA		
Thermodynamics		
SUBJECT AND KEY TECHNICAL WORDS		

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	x Other

ASSOCIATED REPORTS

TR_Hypo 030606 MP.doc

Abstract

For testing the Hypothermia Induction device patient temperature control away from the Safar Center for Resuscitation Research (SCRR) lab, I developed a "Pig Simulator". This is a thermodynamic equivalent to a live subject weighing between 45 and 65 lbs. The heat loss of the "Pig simulator" to the environment is 0.1°C versus the 4°C forced cooling by the hypothermia induction device over 10 minutes time while the patient and inflow/outflow cooling rates are very close to those of a 25 kg pig. The "Pig Simulator" is a very useful tool for temperature testing of the hypothermia device.

Background

The idea of simulating thermodynamically a 45-65 lb live subject is simple for our purposes. We need a bucket filled with warm water that simulates the body with a certain length of tubing coiled inside the bucket and filled with warm water that circulates at a certain flow rate that simulates the blood. But how much water is required in the bucket and how much in the tubing? To answer these questions, we refer to technical report TR_Hypo 030606 MP.doc. To determine the amount of water that contains the same amount of heat as a 25 kg pig we set $\Delta Q_b = c_b\, m_b\, \Delta T$ and $\Delta Q_f = c_f\, m_f\, \Delta T$ equal and solve for m_f. Hence $m_f = m_b\, (c_b / m_f)$. Plugging in numbers (c_b = 2.946 kJ/kg°C, m_b = 25 kg , c_f = 4.196 kJ/kg°C), we get m_f = 17.56 kg or 4.6 gallons of water. Body heat loss is not considered because it is counterbalanced by metabolic heat. Therefore as long as the bucket is well insulated it can be neglected.
A 25 kg pig has approximately 2 L of blood, since the specific heat capacity of blood is equal to water, we calculate the length ℓ of 3/8 ID tubing (LS-18) that can hold a volume of V = 2 L of water as follows $\ell = 4\ V / (\pi\ ID^2)$. Plugging in values we get 92 feet. The fluid must be circulating at 2 L/min to simulate cardiac output.
The bucket must hold 92 feet of tubing that displaces about 0.9 gallons of water plus 4.6 gallons of water or 5.5 gallons.

Introduction

Temperature control testing of the Mild-Moderate Hypothermia Induction device at the Safar Center for Resuscitation Research is expensive and time consuming. If a test subject is simulated thermodynamically, the device then can be tested at Ardiem premises.

Purpose

The purpose of this report is to describe the design and test of a thermodynamic equivalent subject used in temperature control testing of the Mild-Moderate Hypothermia Induction device we nick-name "Pig Simulator".

Description of Apparatus and Setup

I used a seven gallon plastic container with 100 feet of LS-18 inexpensive vinyl tubing, 3/8"ID x 1/2"OD, 50 ft/pack (Cole Parmer EW-06405-12) coiled inside as shown in Figure 1. The bucket lies inside a corrugated box and is padded with common house construction insulation.

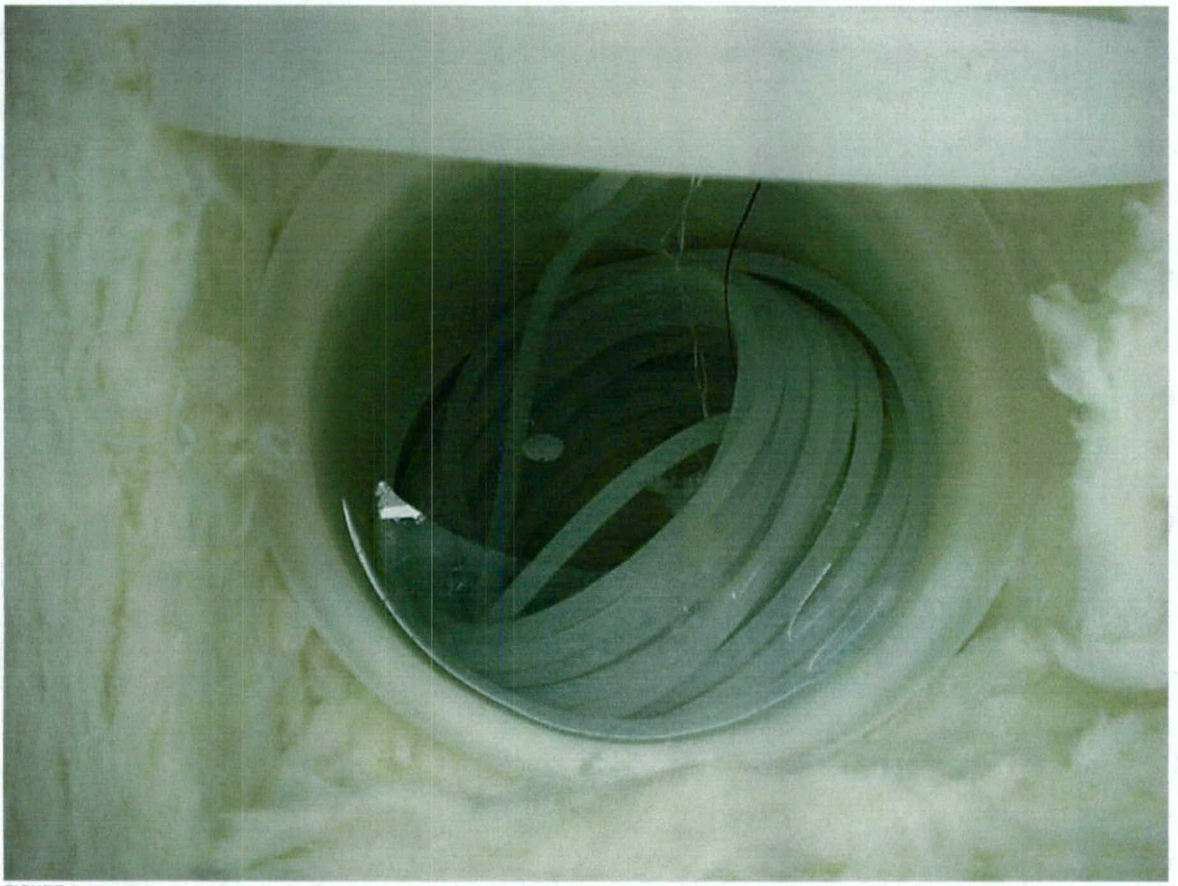


FIGURE 1

I used a Masterflex L/S Digital Standard Drive with a model 7518-10 pump head to circulate the fluid, as shown in Figure 2. I used a pair of plastic T fittings to tap the LS-25 that is used for the cooling system of the device into the LS-18 "blood" circuit. I placed two standard YSI 400 equivalent temperature probes floating in the water to measure PATIENT TEMP 1 and PATIENT TEMP 2 that the device monitors plus the INFLOW and OUTFLOW (with respect to the heat exchanger) temperatures that are also monitored by the device. I also used a Fluke 53 II Digital Thermometer with a K thermocouple probe to get an independent reading of the water temperature.

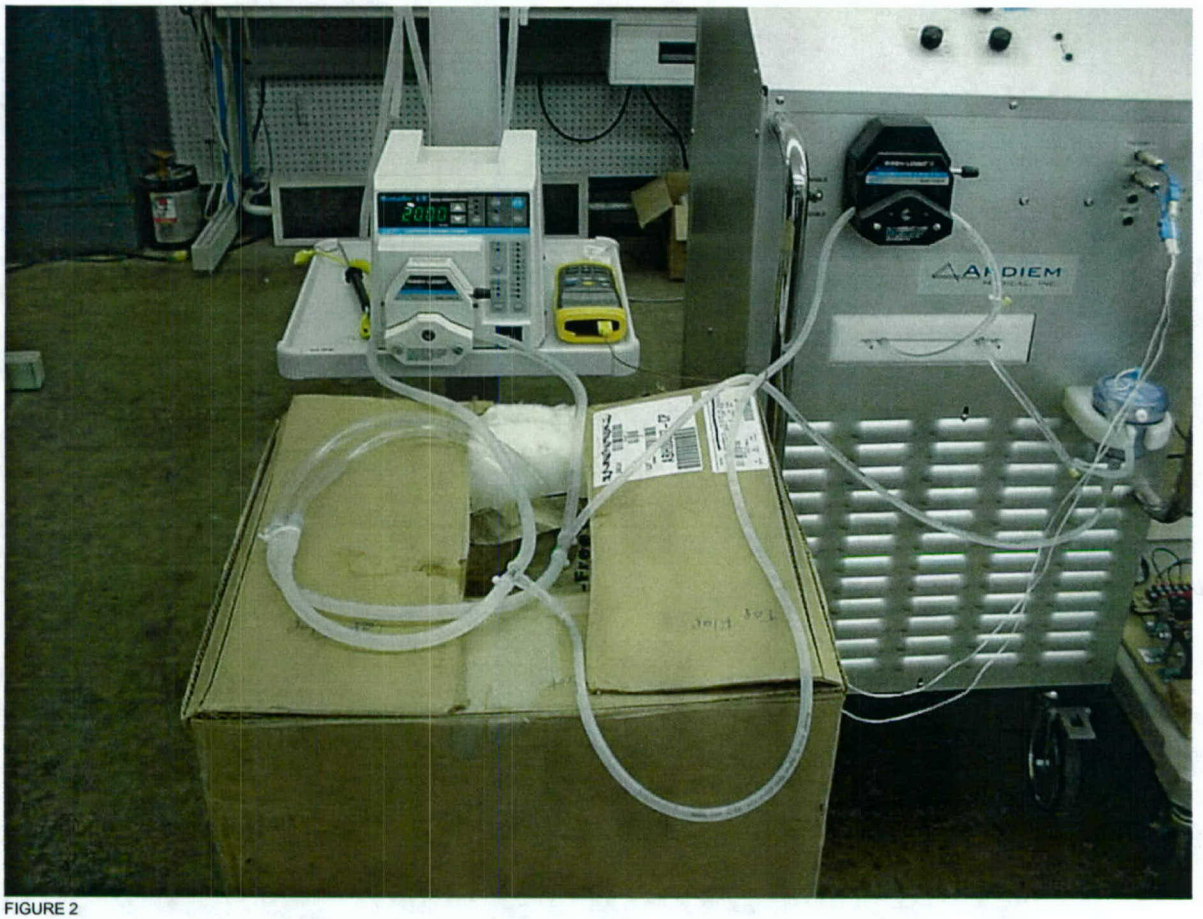


FIGURE 2

Summary of Data and Results

When the temperature probes were placed at close proximity in the water they read the exact same temperature to 1/10 of a degree, the readout resolution of the device.

The "Pig Simulator" environmental insulation was tested by filling the bucket and tubing with warm water and monitoring the water and ambient temperatures with a Yokogawa MV110 recorder over a prolonged period of time while circulating the fluid in the tubing at 2 L/min. The data of this experiment is shown in Figure 3. The temperature drops from 36.1°C to 34.3°C in about 3.7 hours. This represents a heat loss rate of 0.48°C/hour.

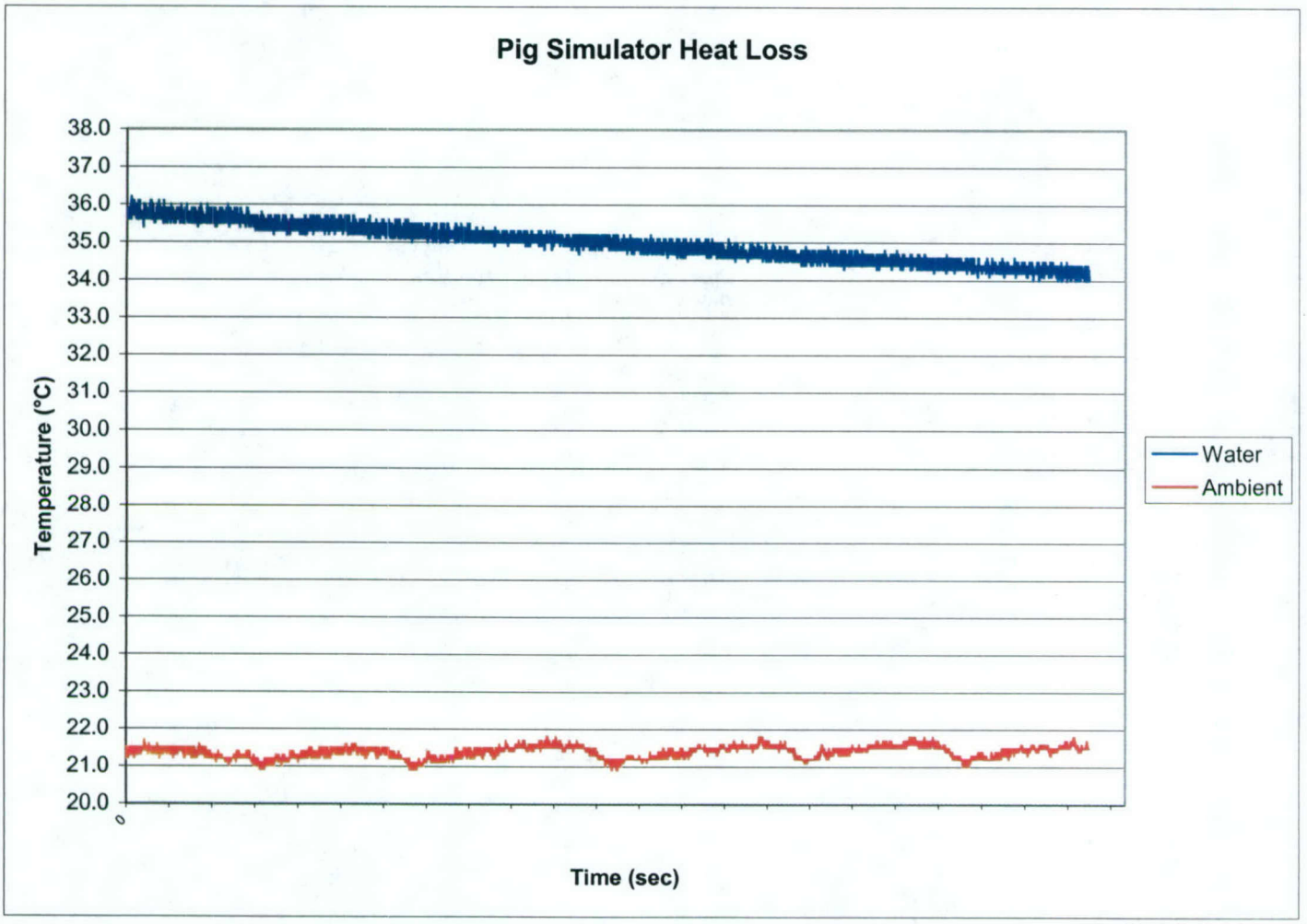


FIGURE 3

Figure 4 and Figure 5 show data taken using the device on the simulator is compared to data taken using the device on a actual pig experiment at the SCRR on 11/14/2003 and also compared to data provided by SCRR during the same pig experiment.

Simulator data is also plotted in Figure 6 and actual pig data taken on 11/25/2003 is plotted in Figure 7 for comparison.

Corresponding PATIENT TEMP 1 and 2 as well as INFLOW AND OUTFLOW temperatures of the "Pig Simulator" are very similar to the actual pig data taken with the device and that provided by SCRR. Ramping and dwelling of these temperatures bears close resemblance.

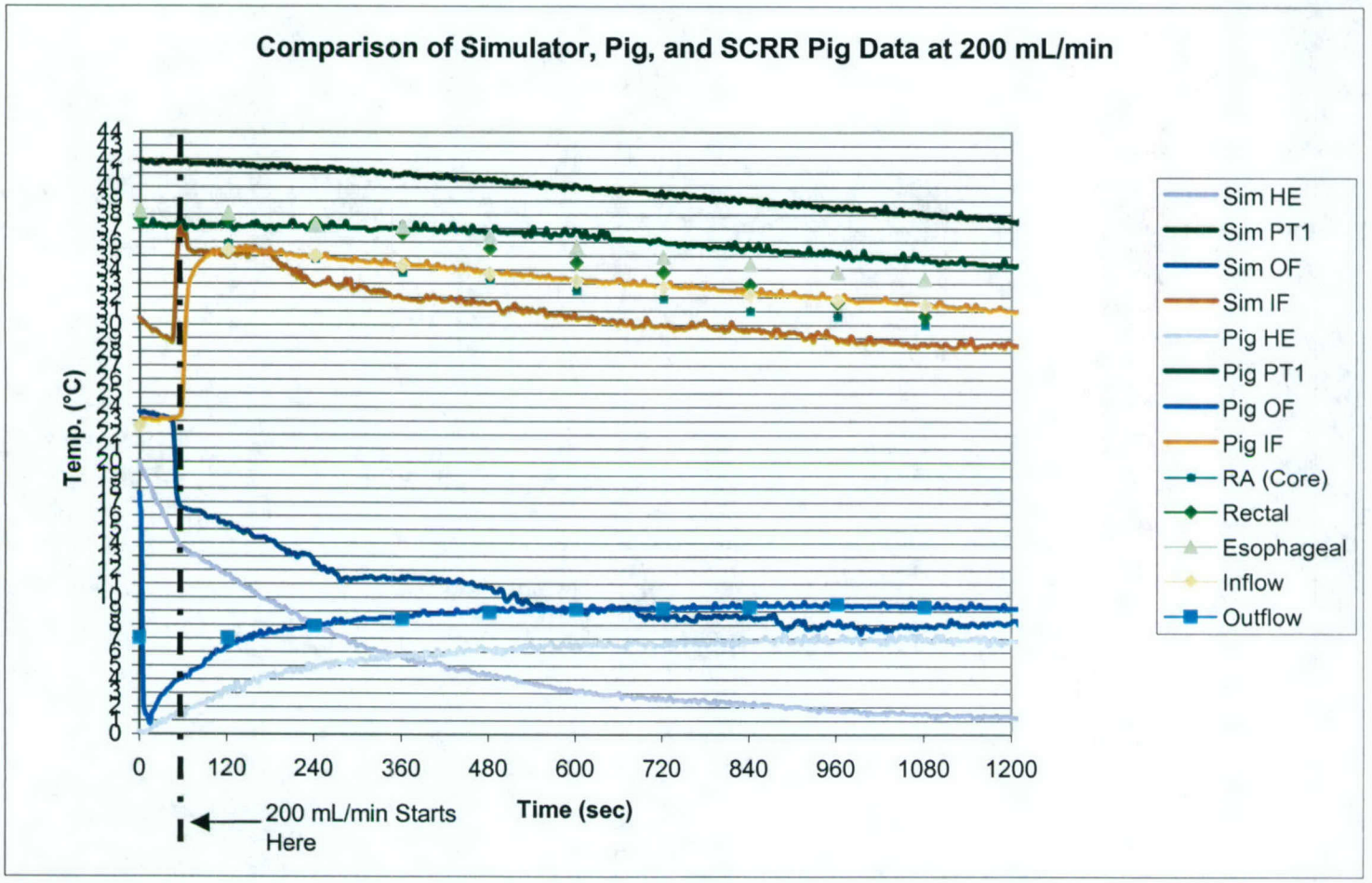

Comparison of Simulator, Pig, and SCRR Pig Data at 200 mL/min
Temp. (°C)
Time (sec)
0
120
240
360
480
600
720
840
960
1080
1200
200 mL/min Starts Here
Sim HE
Sim PT1
Sim OF
Sim IF
Pig HE
Pig PT1
Pig OF
Pig IF
RA (Core)
Rectal
Esophageal
Inflow
Outflow

FIGURE 4

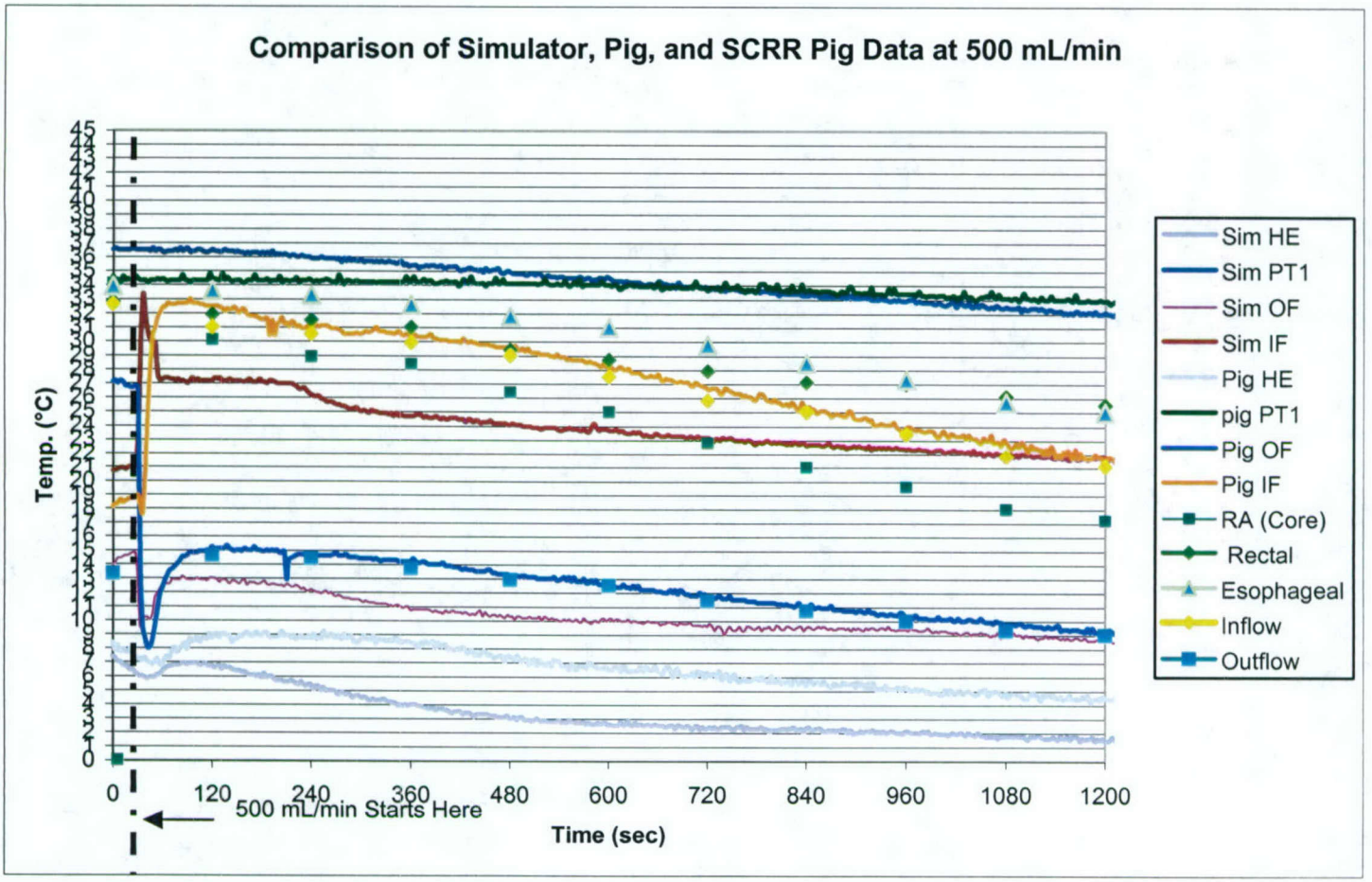

Comparison of Simulator, Pig, and SCRR Pig Data at 500 mL/min
Temp. (°C)
Time (sec)
500 mL/min Starts Here
0
120
240
360
480
600
720
840
960
1080
1200
Sim HE
Sim PT1
Sim OF
Sim IF
Pig HE
pig PT1
Pig OF
Pig IF
RA (Core)
Rectal
Esophageal
Inflow
Outflow

FIGURE 5

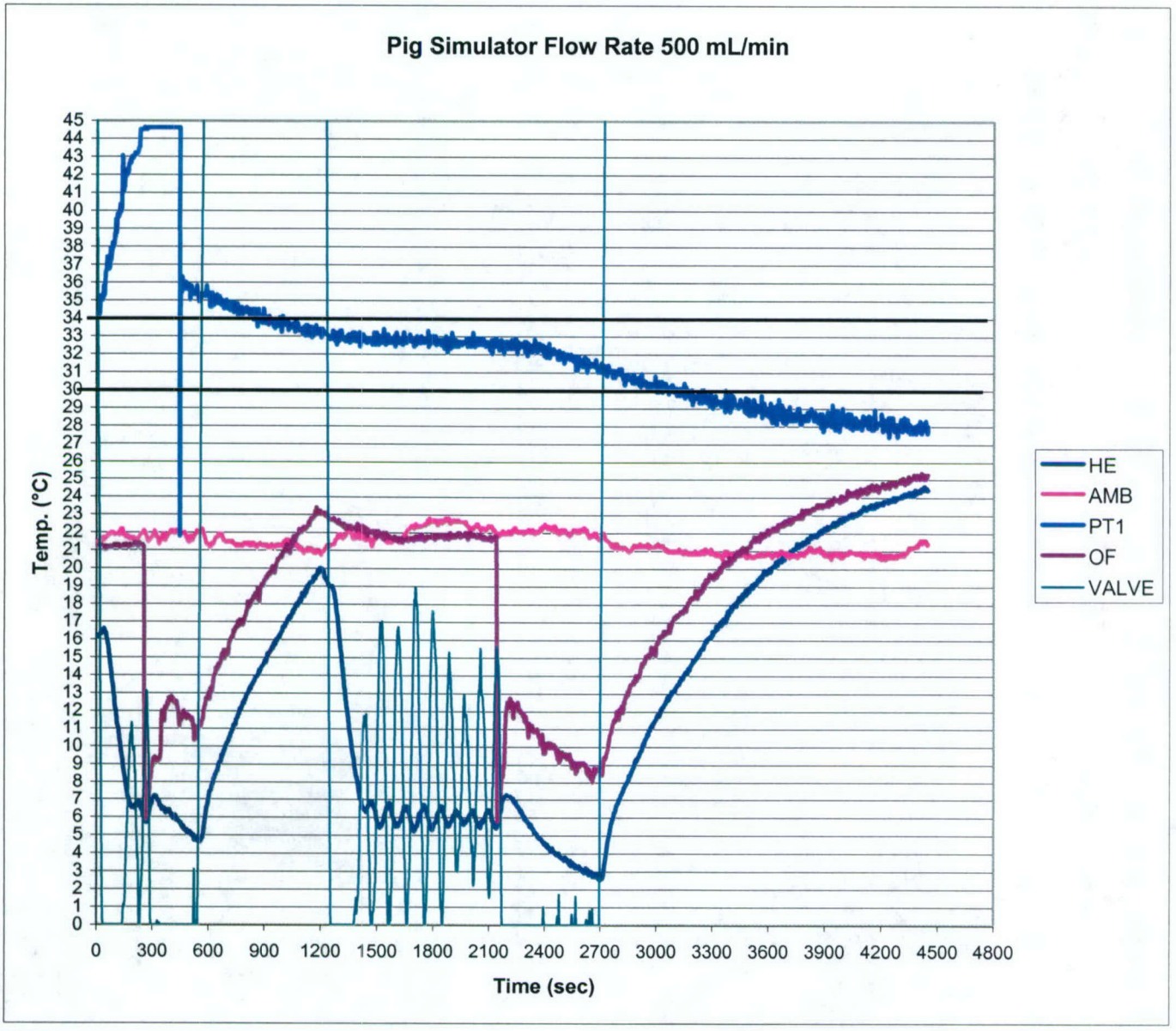

Pig Simulator Flow Rate 500 mL/min
Temp. (°C)
Time (sec)
HE
AMB
PT1
OF
VALVE

FIGURE 6

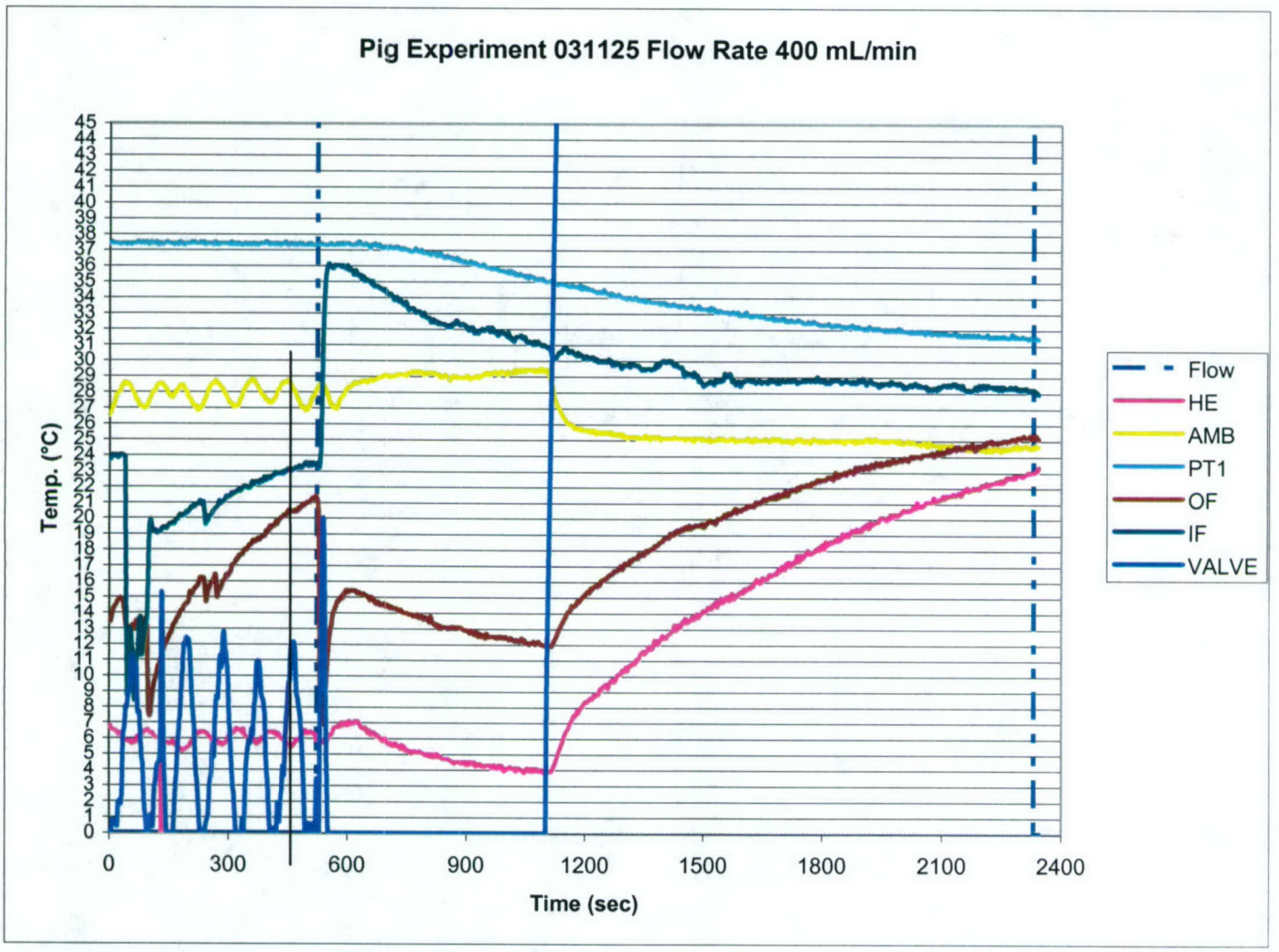


FIGURE 7

Conclusions

The heat loss of the "Pig simulator" to the environment is much slower than the cooling rates used in hypothermia induction. That is 0.1°C versus the 4°C intended drop during the 10 minute procedure time. The "Pig Simulator" patient and inflow/outflow cooling rates are very close to those of a 25 kg pig.

Suggestions for Further Work

No further work is necessary at this point. However before human trials in the future, a 75 kg body should be simulated for device testing.

Appendix W

ARDIEM

TECHNICAL REPORT

RECORD NO.

AM-00013

TITLE OF TECHNICAL REPORT		REVISION
Hypothermia Devices Temperature Calibrator		0
PROJECT OR PROGRAM NAME	PROGRAM NUMBER	DATE
Hypothermia	2004-02	04/22/04
DESCRIPTION OF TASK PROMPTING TECHNICAL REPORT	NAME OF AUTHOR	
	Mike Pitsakis	

TECHNICAL AREA

Test, Measurement

SUBJECT AND KEY TECHNICAL WORDS

Hypothermia

DOCUMENTATION TYPE

☐ Validation	☐ Error Budget	☐ Reliability	☐ Sensitivity
☐ Verification	☐ Product Support	☐ Risk Analysis	☒ Other

ASSOCIATED REPORTS

Abstract

I designed a temperature calibrator to be used in testing the temperature electronics of the hypothermia devices. The calibrator accuracy was tested with a NIST traceable instrument and passed. The calibrator is ready for use.

Background

In experimental, engineering, and future production devices, testing the circuits for temperature accuracy is very important.

Introduction

I designed and constructed a temperature calibrator using 1% tolerance fixed resistors to simulate a YSI 400 temperature probe (thermistor) at different temperatures. The calibrator is to be used in determining the accuracy of the electronics in measuring temperature.

Purpose

In writing this report, I aim to explain the usefulness, operation, and accuracy of the calibrator.

Description of Apparatus and Setup

The schematic of the calibrator is shown in Figure 1.

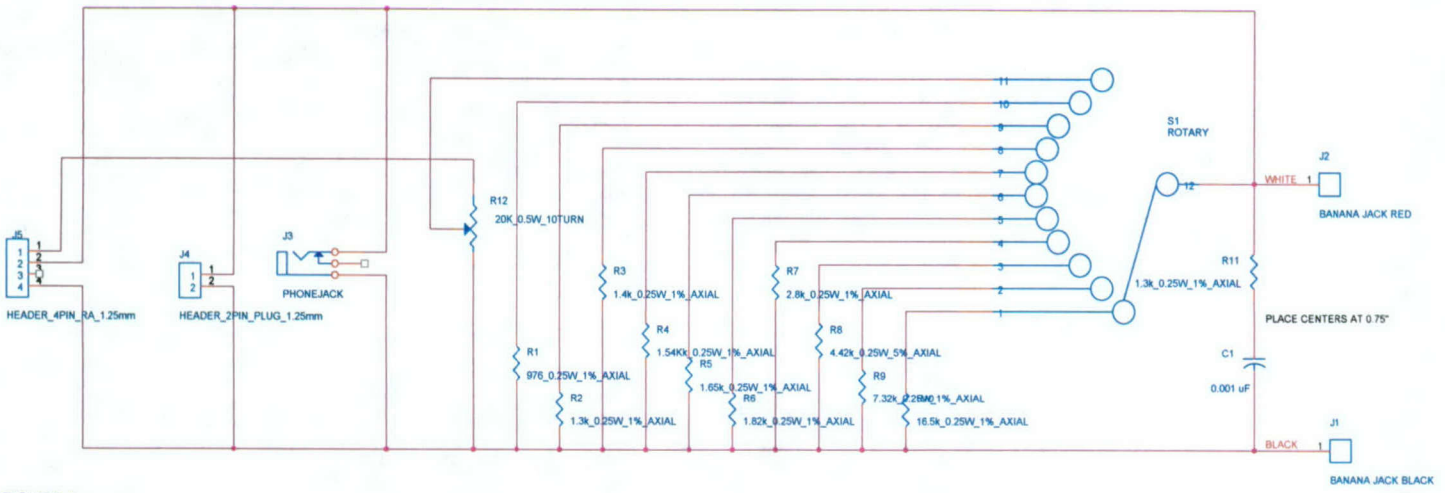


FIGURE 1

It has a number of outputs J1 – J4 that connect to a fixed resistor depending on the selection by the rotary switch position. Each position corresponds to different resistance value and therefore a different "temperature". The 11th position is reserved for a potentiometer that can be set to any resistance form 0 – 20 K and cover –80 to 250 °C. The resistance of the potentiometer may de determined by measurement between J1 and J2 banana connectors. J3 is a phone jack, the standard connector of YSI 400 compatible temperature probes (Thermistor Mix "B" 2252 Ω @ 25°C). The resistance value for each selection of the pot was also measured using an accurate DMM Fluke 75/23II (±0.5%). The corresponding temperate was calculated using the Steinhart-Hart equation over the range of –15 to 45°C modeled in spreadsheet. \\ARDIEMFS\RD\5-Engineering\Systems Eng\Hypothermia\Analysis\Model_Therm YSI.xls
With the following coefficients:

A=1.467140056809390E-03
B=2.384088270851750E-04
C=1.009987514947380E-07

In the experiment, I connected J3 of the calibrator to the input of a YSI400A precision thermometer (NIST traceable) and recorded the temperature reading for each pot position. The YSI400A specifications are listed below together with specifications of standard compatible probes.

YSI PrecisionTM 4000A Thermometer
Temperature Display Range 0 to 50°C (32 to 122°F selectable)
Accuracy ± 0.10°C (0.20°F) in the range between 25 and 45°C (77 and 113°F)
± 0.20°C (0.40°F) throughout the rest of the measurement range
Resolution 0.01°C (0.01°F)
Input YSI Precision TM 400 Series Reusable Probes or YSI Precision TM 4400 Series Disposable Probes
Probe Power Typically 30 microamps or less, depending upon temperature being measured
YSI 400/700 Series Reusable Temperature Probes
Temperature Range 0 to 60°C

Accuracy ±0.2°C from -1 to 60°C, ±0.1°C from 25 to 45.2°C

Summary of Data and Results

The table shown in Figure 2 summarizes the measured and calculated values for each switch position. There is a small deviation between temperature readings that must be due to the YSI400A accuracy. The calculated temperature values based on actual resistance readings are accurate to ±0.02 °C (worst case algorithm error over range[1]).

Switch Position	Measured Resistance (Ohm)	Measured Temp. w/ YSI4000A (°C)	Calculated Temp. Based on Resistance Reading with Spreadsheet (°C)	Percentage Deviation
1	973	45.26	45.28	-0.05
2	1297	38.06	38.07	-0.02
3	1395	36.30	36.28	0.05
4	1533	34.02	34.00	0.05
5	1641	32.40	32.37	0.08
6	1813	29.99	30.02	-0.09
7	2794	20.17	20.15	0.08
8	4400	10.39	10.39	0.03
9	7290	0.31	0.17	44.15
20	16440	Over range	-15.01	

FIGURE 2

Note that theYSI400A demonstrates a large error of 44.15% at 0°C the end of its range.

Conclusions

The calibrator is accurate and should be used as reference in testing the temperature electronics. Any deviation beyond ±0.02 °C will be due to amplifier gain error or A/D quantization error.

Suggestions for Further Work

No further work is necessary.

[1] Determined comparing spreadsheet values to table values given by YSI.